THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 168, NO. 16 — CHICAGO, ILLINOIS — DECEMBER 20, 1958

COPYRIGHT, 1958, BY AMERICAN MEDICAL ASSOCIATION

NEUROSURGICAL CARE OF THE SEVERELY INJURED PATIENT

Guy L. Odom, M.D., Durham, N. C.

The frequency and gravity of injuries to the brain and spinal cord are such that they must be considered in the neurosurgical treatment of every seriously injured patient. It is necessary to recognize shock when it exists, for it must receive priority over everything else except when there is evidence of extradural hematoma. Shock is rarely caused by head injuries alone; its existence should immediately direct the examiner's attention to other parts of the body. The blood pressure, pulse rate, respiration rate, and temperature should be recorded every 15 minutes at first; at the same time the pupils should be observed as to size and reaction to light, and the state of consciousness must be determined. Extradural hematoma, if it occurs, requires immediate surgical intervention; if it is neglected, the results are either death or irremediable deficits. The immediate recognition of a spinal injury is of extreme importance in order to prevent further damage to the spinal cord. It is especially liable to be overlooked in the unconscious patient, and the transportation of such patients requires the greatest care. Surgery of compound depressed skull fractures can be delayed until the patient's vital signs are stable, and immediate laminectomy for spinal cord injuries is seldom required.

IT HAS BEEN estimated that injuries to the head occur in 72% of persons involved in automobile accidents and that 1 out of every 10 such injuries is dangerous or fatal.[1] These appalling figures indicate that the general practitioner and general surgeon must have adequate knowledge of handling the severely injured patient from a neurosurgical standpoint if the morbidity and mortality are to be reduced. The steady increase in the accident rate, despite the publicity of safety methods advocated by Shelden [2] and various organizations, indicates that the medical profession must continue to carry this gruesome burden.

It is impossible to adequately review all the problems encountered from a neurosurgical standpoint, and, therefore, I will confine my remarks to the decisions that must be made shortly after the patient is first seen and to treatment of acute emergencies.

Craniocerebral Injuries

It is frequently difficult to make a definite diagnosis or to completely evaluate a patient from a neurological standpoint immediately after an injury. In this complex situation one must, however, determine whether the patient is in shock, whether multiple injuries have occurred, whether there is evidence of increasing intracranial pressure, and whether there is evidence of spinal cord involvement.

The problems of shock and multiple injuries can be discussed together, because a severe head injury alone is seldom responsible for a state of shock.

From the Neurosurgical Division, Duke University Hospital and School of Medicine.

Read in the Panel Discussion on Management of the Severely Injured Patient before the General Scientific Meetings at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23, 1958.

This should immediately direct the examiner's attention to the other organs of the body. Braunstein [1] reports that 44% of the patients with head injuries also have injuries to other parts of the body. The rupture of an abdominal organ or intrathoracic bleeding should always be considered in every patient with head injury who is in shock. The examination should also include a careful check of the extremities for long bone fractures to avoid fat emboli during movement. Multiple injuries of this type may be overlooked by the inexperienced examiner due to the fact that he becomes more concerned with the impairment in the patient's state of consciousness. The treatment of shock demands priority over everything else, u less it is obvious that the patient has an extradural hematoma. While the usual methods are being carried out to combat shock, the patient should not be moved for x-rays and scalp lacerations should not be sutured. The wound should be covered with sterile dressings and a tight elastic bandage applied. Most scalp bleeding can be controlled in this manner. In large arterial bleeders, the vessels may have to be clamped or ligated. If a fracture of an extremity is encountered, a temporary splint is applied.

Only after the patient's condition has stabilized can the necessary surgical procedures be carried out or the patient transported to another center.

The maintenance of an adequate airway is as essential as treating shock. The air passages may become obstructed by blood, mucus, and vomitus. This can be avoided by positioning the patient on his side with the head slightly lowered in order that dependent drainage may occur. At times suction is necessary, and, in patients with extensive faciomaxillary injuries, tracheotomy may be a lifesaving procedure. One should never hesitate to perform a tracheotomy in the unconscious patient who is having difficulty with respiration and is requiring frequent suction. Patients should not be transported unless someone is in constant attendance to prevent the aspiration of vomitus.

Observation and Treatment

After the first-aid procedures discussed above, if a closed head injury is present it may be necessary to observe the patient to determine whether the problem will be surgical or nonsurgical. The decision depends on whether the patient develops signs of increasing intracranial pressure.

The blood pressure, pulse rate, respiration rate, and temperature should be recorded every 15 minutes for one to two hours, then every 30 minutes, and finally every hour depending on the individual case. Elevation of the blood pressure, slowing of the pulse rate, rising temperature, and irregular respirations are indications of acute increased intracranial pressure.

Each time that the vital signs are recorded, the nurse should check the patient's state of consciousness. In the comatose patient, painful stimulation to the extremities should be used to determine whether there is less motor response on one side than the other.

The pupils are observed as to size and reaction to light each time the patient is checked. Unilateral dilation of the pupil followed by fixation is indicative of third nerve compression from herniation of the medial aspect of the temporal lobe over the edge of the tentorium. Bilateral constricted and fixed pupils and extensor rigidity of the extremities immediately after injury suggest mid-brain involvement and extremely poor prognosis.

If the patient is comatose, his position should be changed every two hours, an indwelling catheter should be used to avoid distention of the bladder and soiling the bed clothes, and he should be given fluids intravenously, 3,000 cc. daily (1,000 cc. of 5% glucose in saline solution and 2,000 cc. of 5% glucose in water), first for several days and then nasal feedings (electrolytes should be checked every two to three days). If the temperature becomes elevated, bed sheets and pajamas should be removed and an electric fan directed on the patient. Aspirin may be given by rectum, and, if necessary, cracked ice may be placed on a sheet over the patient. If patient is restless, 20-30 cc. of paraldehyde is given by rectum. Morphine should be avoided in all head injuries. Sodium phenobarbital, 60 mg. (1 grain), given intramuscularly every four to six hours is used to control convulsive seizures.

Extradural Hematoma

An extradural hematoma is one craniocerebral condition which requires immediate surgical intervention as soon as suspected if the patient's life is to be saved or marked residual neurological deficits prevented. Everyone who has had a transient episode of loss of consciousness should be observed for the first 12-24 hours with this possible diagnosis in mind. This is especially true if the accident occurs at night or if there has been an intake of alcohol. If the patient refuses hospitalization, a responsible relative or friend should be carefully instructed as to the situation and advised to rouse him every 30 minutes during the remainder of the night.

Extradural hemorrhages are caused by a linear fracture in the temporal region tearing the middle meningeal artery. The blow may have produced a short period of unconsciousness, but this is not so in every case. The hematoma with brain compression develops rather rapidly due to the arterial bleeder and sets up a chain of events which have

already been discussed from the standpoint of increased intracranial pressure. The patient who has been clear mentally after an initial period of unconsciousness will become confused or semistuporous, his voluntary movements will become less pronounced on one side of the body, and his blood pressure will become elevated, with slowing of the pulse rate. It is at this stage that the diagnosis should be made and exploratory trephination performed. If the hematoma is not evacuated within a short period of time, coma will develop and the pupil on the involved side will become dilated and fixed to light from compression of the third nerve by a hippocampal herniation. If the patient has been permitted to reach this stage, immediate operation should be performed. There should be no delay for x-rays or even waiting for the patient's condition to stabilize if he is being treated for shock. The procedure is carried out with use of local anesthesia, and the usual methods can be continued to combat shock in the operating room. If a neurosurgeon is not available, the operation should be performed by a general surgeon. Valuable time will be lost in transporting the patient to another hospital, where he may be dead on arrival or irreversible damage to the brain stem may already have occurred. The later changes are due to the fact that the hippocampal herniation not only compresses the third nerve but also obstructs the spinal fluid pathway, which further increases the intracranial pressure. The herniation then enlarges with compression of the posterior cerebral artery, an infarction of the occipital lobe. Herniation of the opposite hippocampal gyrus will occur and both pupils become dilated and fixed to light. At this stage, brain stem involvement occurs with bilateral extensor rigidity of the extremities. The terminal phase of this sequence of events is hemorrhage into the brain stem. If a patient has developed bilateral dilated and fixed pupils, his prognosis is hopeless. The chances of survival even if the hematoma is evacuated and the herniation removed or tentorium split are nil.

It is always wiser to carry out exploratory trephination in the temporal region as soon as one suspects the possibility of an extradural hematoma by change in state of consciousness rather than to wait for evidence of a hippocampal herniation. Both temporal regions should be explored if the procedure is performed before localizing signs occur. If there are focal signs and a hematoma is not encountered on the suspected side, trephination should always be done on the opposite side. X-rays may be extremely helpful, if they have been obtained, by revealing a linear fracture crossing the middle meningeal groove or a shift of the pineal gland.

After evacuation of an extradural hematoma in the patient with third nerve palsy, the medial aspect of the base of the temporal lobe should be explored for a hippocampal herniation. If it has been present for a short period of time, it may be forced upward by injecting Ringer's solution into the spinal canal. If this fails, the herniation should be removed by suction or the medial edge of the tentorium should be split for a distance of 1.5 cm.

An acute subdural hematoma or extensive contusion and edema of the temporal lobe will produce a clinical picture which may be difficult to differentiate from that of an extradural hematoma. In the former, however, there is usually a history of a more severe injury and patient's state of consciousness is impaired from the time of the accident. Because of these possibilities, if an extradural hematoma is not encountered at the time of the exploratory trephination, the opening should be enlarged so that the subdural space and temporal lobe may be explored. At times, it is necessary to remove a portion of the contused temporal lobe because the softened edematous lobe may have herniated over the edge of the tentorium.

Compound linear and compound depressed fractures and penetrating wounds seldom require immediate surgical intervention, and operation can be delayed until the patient's vital signs are well stabilized and injuries to other parts of the body have been treated. Space does not permit a detailed description of the surgical procedures, but the following points must be stressed. The entire scalp should be clipped and shaved widely about the involved area; thorough cleansing and débridement of the scalp edges should be done; exposed linear fractures should be thoroughly inspected for hair and foreign material caught between edges of bone; and if foreign material is present the bone along both edges of the fracture line should be removed. In cases of compound depressed fractures, the bone fragments should be removed and cranioplasty performed at a later date. Depressed fractures over the large venous sinuses should not be elevated unless an exposure of the sinus on both sides of the fracture has been carried out in order that the bleeding from the sinus can be controlled if it has been torn. If the dura and cortex have been lacerated, a tight closure of the dura should always be obtained. In penetrating wounds, lumbar drainage of spinal fluid to decrease intracranial pressure is helpful in exploration of the missile tract.

Spinal Injuries

The immediate recognition of a spinal injury is of extreme importance in order to prevent further damage to the spinal cord. This is seldom a problem in the conscious patient, but it must be remembered that the unconscious patient may also have sustained an injury to the spine and spinal cord. In the comatose patient, the absence of deep reflexes in the lower extremities, diaphragmatic respirations, and the failure to obtain any reflex movement to painful stimulation in the lower portion of the body and to do so over the arms or shoulders indicates involvement of the spinal cord.

In all suspected spinal injuries, proper transportation is essential. This also applies to conscious, nonparalyzed patients who may complain of neck or back pain or numbness or pain in an extremity or extremities. More damage may be done to the cord by jackknifing the back or flexing the neck during transportation by an enthusiastic sympathizer than at the time of the original injury. The patient should not be lifted unless sufficient assistance is available to prevent flexion of the spine, and he should be placed on a firm, flat stretcher. Patients with injuries to the cervical spine do better on the back with sandbags or some other object along the side of the head and neck because of the diaphragmatic respirations. Those with lumbar or thoracic fractures may be placed on the abdomen.

As in head injuries, treatment of shock and maintenance of adequate airway assume prime importance. Intranasally administered oxygen should be used in all patients with cervical cord injuries, and, at times, immediate tracheotomy should be done if the injury is at the mid-cervical level. If the vital signs are stable, adequate x-rays should be obtained as soon as possible. In patients in whom cervical injury is suspected, the shoulders must be pulled down to obtain adequate exposure of the seventh cervical vertebra and views should also be taken of the odontoid process. The patient remains on the x-ray table while the films are being developed, and at this time he may be rolled on his side and a manometric examination carried out to determine whether there is a block in the subarachnoid space. As soon as the films are developed, a decision can be made as to the next step of relieving cord compression and reducing a fracture dislocation.

Cervical fracture dislocations can be reduced in a matter of hours by means of Crutchfield tongs with 20 to 40 lb. of traction. One should begin with 20 lb. and obtain periodic portable films to follow the reduction. The weights are gradually increased, depending on the case. After reduction, the patient is left in traction but the weights reduced to 10 to 15 lb.

In patients with cervical injuries who require immediate surgery of some other part of the body, tongs and traction should be applied before proceeding with the operation.

An indwelling catheter should be inserted shortly after admission and, if abdominal distention occurs, Miller-Abbott and rectal tubes should be used.

Laminectomy is seldom performed as an emergency procedure in closed injuries to the spinal cord and, in fact, may be an added unnecessary risk, especially in patients with injuries to the cervical cord. If a complete reduction cannot be accomplished by traction, an open reduction can be done a week or so later.

Fractures of the lumbar spine with involvement of the cauda equina present a different problem than fracture dislocations in the cervical and thoracic regions. If there are not other serious injuries, surgical decompression of the roots of the cauda equina will give a better prognosis.

In penetrating and gunshot wounds, operation is performed as soon as the patient's general condition will permit. The depressed bone fragments and foreign material are removed and the lacerated dura closed.

Summary

In care of the severely injured patient from a neurosurgical standpoint, one must determine first whether the patient is in shock, second, whether there are multiple injuries, third, whether there are signs of increasing intracranial pressure, and, fourth, whether there is evidence of spinal cord involvement. Shock must receive priority in treatment, except when there is evidence of an extradural hematoma. Maintenance of an adequate airway is important. Surgery of compound depressed fracture can be delayed until patient's vital signs are stable.

Attention must be paid to signs of spinal cord involvement in the unconscious patient. Further, the patient must be protected from additional cord damage during transportation. Spinal cord injuries seldom require immediate laminectomy.

References

1. Braunstein, P. W.: Medical Aspects of Automotive Crash Injury Research, J. A. M. A. 163:249-255 (Jan. 26) 1957.

2. Shelden, C. H.: Prevention, Only Cure for Head Injuries Resulting from Automobile Accidents, J. A. M. A. 159:981-986 (Nov. 5) 1955.

CARE OF THE PATIENT WITH MULTIPLE INJURIES

Otto E. Aufranc, M.D., Boston

In dealing with an extensively injured patient, the most immediate problems consist of preventing asphyxia, stopping hemorrhage, replacing blood, and avoiding damage during transportation. The physician who first examines the patient must be systematic, and after the immediately evident problems have been dealt with the less obvious injuries must be considered. Fractures of extremities are overlooked in some cases; in others they hinder the physical examination and may divert the examiner's attention from serious spinal, intra-abdominal, or intrathoracic injuries. Sucking wounds of the chest, severe uncontrolled hemorrhage, and penetrating wounds of the abdomen require emergency operation. When combined abdominal and thoracic injuries are encountered, the thoracic portion is undertaken first. In many situations prompt action is more important than specialized knowledge, and such measures as clearing the airways by aspiration or tracheotomy, closure of open chest wounds, transfusion, splinting, or amputation may be lifesaving.

There can be no rigid rules for the management of all extensively injured patients. The early recognition and management of important unsuspected lesions, however, will help to prevent additional superimposed trauma which, in itself, may make the difference between life and death or between mere survival and independence. The most important immediate problems consist of recognizing or establishing an adequate airway, preventing further hemorrhage, replacing blood, and avoiding damage by injudicious movement of the patient or his injuries.

Immediate Measures

We all know that the movement of the patient from the site of injury can itself be the actual cause of death. Transportation should be undertaken by trained persons, and those who do not know what to do should not do anything except try to get additional help. Transportation with the simplest type of side-splinting is probably the best. The control of hemorrhage by direct pressure compression bandages as opposed to a tourniquet is probably also best. Movement of the patient from the site of injury to the hospital should not be done with great speed but with great care and gentleness. Sudden starts and stops, bouncing over rough roads, and swerving around corners cannot do the injured patient any good.

Establishment of Extent of Injury.—The physician who first examines the patient should do a complete, rapid physical examination by a system, being sure in his own mind what he should look for. As with any physical examination, looking for the normal immediately reveals the abnormal. We should use all the senses we have been taught to use. We should look, we should feel, we should smell (alcohol, vomitus, feces, and urine acetone), we should listen, but, most of all, we should think.

A simple recording of the clinical findings is essential, since the clinical course of the patient and progressive changes of signs and symptoms are often the actual key to correct diagnosis. Recording of important negative findings which later change to positive makes a different prognosis. This is particularly true of intra-abdominal, head, and chest injuries.

Evidences of certain traumas are obvious to anyone. However, a more serious injury may be undetectable at the initial examination. Visceral injuries of this nature frequently manifest themselves hours after the initial trauma. They must be specifically suspected and specifically looked for in order for the physician to be ahead of their devastating possibilities if they are found out too late.

The orthopedist is taught to suspect a combination of injuries in certain types of trauma. For example, fractured patella and dislocation of the hip are often combined. The os calcis fracture is also often associated with a central dislocation of the hip or a fracture of the spine or of the base of the skull or both. A crushed pelvis is frequently combined with a rupture of the posterior urethra. Chest injuries are often associated with a ruptured spleen or a diaphragmatic hernia, and penetrating chest wounds may and often do involve abdominal viscera. These combinations must be thought of in order not to be overlooked.

Asphyxia, severe hemorrhage, and shock are common features in multiple injury cases, and immediate recognition and treatment are necessary. First, an open airway is essential to life and must be provided for at once. Simple manipulation of the tongue, mandible, or both or the change of position of the head and neck may be all that is necessary in the semiconscious or unconscious patient. Suction applied to or wiping out the upper airways

From the Department of Orthopedic Surgery, Harvard Medical School.
Read before the General Scientific Meeting at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23, 1958.

may be sufficient to remove blood or mucus to establish a normal rate of respiratory exchange. At times, however, a tracheotomy must be resorted to as a lifesaving measure. It should be resorted to more frequently than the "wait and see" method when the patient seems to be in extreme condition. In those patients who do not have a cough reflex for clearing the upper passage, suction and administration of oxygen through a tracheotomy tube can be maintained with ease and infinitely more efficiently than by any other method.

Control of Hemorrhage.—Gross hemorrhage is the most common and often the simplest of all the conditions to alleviate. The application of local pressure, the use of the hemostat, and ties on grossly bleeding, pulsating vessels will control bleeding. However, pressure dressings carefully packed by the experienced surgeon are probably as efficient as any method of controlling hemorrhage. Such things as previously applied tourniquets and dressings should be removed so that the hemorrhage may be estimated and one can be more definitely sure that further loss of blood may not be a part of the maintenance of a shocked state. Concealed hemorrhage in the thorax, abdomen, or retroperitoneal space may cause death. In the severely injured patient, blood replacement therapy should be initiated at once and, while replacement of blood is being brought about, a more careful evaluation of the patient is easier and more surely apt to save his life—continued massive hemorrhage is not compatible with life for even a short duration of time.

The arrest of hemorrhage in the extremities probably deserves a specific note. Simple adequate elevation of the arm or leg often stops hemorrhage. In most cases arrest of hemorrhage might be better brought about by the use of a hemostat. However, the blind application of the hemostat to bleeding vessels is to be condemned, as the clamping in a sea of blood may well destroy arterial tissue that might not otherwise be destroyed and may preclude an otherwise reparable suture of a major vessel. Major nerve trunks usually accompany major arteries, and a previously damaged nerve may be permanently injured by blind clamping.

The use of a tourniquet when applied by an expert, of course, is invaluable. It requires precise application to arrest all arterial flow. Often tourniquets only obstruct the venous return and thus increase the bleeding. If the tourniquet has been applied and is adequate, it should be left in place until someone can adequately inspect the wound and determine the cause of the hemorrhage. At such a time when blood replacement is possible, several hours can elapse, if the extremity is kept cool, without really damaging the limb.

The amount of blood lost by a patient with a fractured thigh, for instance, may be excessive even though that might be the only injury. The blood loss may be excessive in relation to the loss from circulation. An increase in thigh measurement of 2 in. or more usually means that perhaps as much as 1,500 to 2,000 cc. of blood has been lost in that thigh. With musculoskeletal injuries of both legs and arms, for instance, as much as 3,000 to 4,000 cc. of blood might be lost to the circulation by the swelling and the hemorrhage around the fracture sites themselves.

As soon as an adequate airway has been established, hemorrhage arrested, and blood replacement started, the obvious fractures should be splinted to prevent further trauma and shock. Major fractures, strangely enough, are commonly overlooked. Minor fractures and, frequently, dislocations of the major joints may go undetected. Fractures must be reduced and splinted not only to insure union and function but, mainly, to combat shock.

Shock.—Shock of some degree is associated with all multiple injuries. The main cause of shock is often loss of circulating blood volume. Replacement therapy, to be effective, must be prompt. It is best done by the use of whole blood, which increases circulating fluid volume, as well as the number of erythrocytes, to handle oxygen and carbon dioxide requirements in the tissues. Saline solution is invaluable as a temporary agent for raising the blood pressure only while awaiting plasma or whole blood. It should be only used in emergencies, because it leaves the circulation rapidly and takes plasma protein with it. Dextrose in water, as well as saline solution, is essential in treatment of shock.

Since it is important to allow prompt treatment of wounds which have caused the shock, it is essential to replace the missing blood before undertaking the management of the injury. This can usually be undertaken soon after the rise of blood pressure to over 80 mm. Hg with a fall of pulse rate and return of color and warmth to the skin. Blood replacement must be continued throughout the early surgical treatment as necessary. Trendelenburg position of the patient, elevation of the extremities, and the administration of oxygen are all useful adjuncts to the treatment.

Physical Examination.—Some of the diagnostic problems clarify themselves through the usual methods we have been taught, such as taking a good history and doing a careful physical examination. The knowledge of the mechanism of injury may give a real clue to concealed pathological changes. The obvious injuries must not divert the concentration of the careful examiner and thus allow him to overlook other things, such as serious spinal, intra-abdominal, or intrathoracic injuries. The fracture of an extremity and its obvious deformity often detracts from a careful physical examination. For instance, fractures of the extremity or bleeding from head lacerations often attracts attention to such a degree that frequently these are investigated too thoroughly by x-ray and other studies while the obvious but infinitely more im-

portant areas and serious internal injuries may go undetected. One must always guard against too many x-ray examinations when the general physical examination would have done just as well, if not better.

The physical examination must be quick, gentle, and without undue exposure. X-rays should be taken only when necessary and with minimum movement of the patient. It is possible that movement from a stretcher or table to an x-ray table will produce a profound circulatory collapse. It is much better to treat the patient as he is without x-rays rather than be forced to delay urgent therapy because of more shock induced by the performance of an x-ray examination. Roentgenograms for essential diagnosis and correct management can be more safely taken in the emergency room without moving the patient.

Initial Management of Specific Types of Injury

Immediate first-aid measures include control of asphyxia and hemorrhage, management of shock, and temporary splinting of fractures. The surgeon must then focus his attention on specific injuries and treat them with priority in regard to immediate and ultimate management. A decision must be made as to what operative procedure should be undertaken and when. Obviously, sucking wounds of the chest, severe uncontrolled hemorrhage, and penetrating wounds of the abdomen require emergency operation. It is essential to remember that an appreciable number of patients will require formal surgical measures as an integral part of their resuscitation.

Chest injuries require priority in treatment of any serious disturbance of the cardiovascular physiology. Potential bronchial secretions, sucking wounds, pneumothorax, massive bleeding into the pleura, and cardiac tamponade all may lead to profound cardiorespiratory changes requiring immediate treatment. Thoracic injuries should be treated before other operative procedures are undertaken, and when combined abdominal-thoracic injuries are encountered, the thoracic portion is undertaken first.

Crushing injuries of the chest associated with multiple rib fractures and paradox movement of the portion of the thoracic cage present a particularly difficult problem because of the serious derangement of cardiorespiratory physiology. Tracheotomy is particularly valuable in such patients. Paravertebral block and local infiltration to control pain are effective in the maintenance of an adequate oxygen exchange.

Abdominal Injuries.—Blunt and penetrating types of trauma produce many lesions in the abdomen. A careful local examination of the abdomen must be undertaken, particularly in an unconscious patient. All penetrating wounds of the abdomen should be explored as soon as the general condition permits. Watchful waiting is dangerous. Blunt injuries are a little more difficult but are, nevertheless, serious. Ruptured spleen, bladder, lacerations of the liver and intestine, mesenteric hemorrhage, and other injuries to the pancreas all present diagnostic difficulties as a result of blows in the lower part of the chest or the abdominal wall. Lacerations of the kidneys and serious retroperitoneal hemorrhage may be associated with injuries to the spine.

Urologic Wounds.—Urine specimens must be obtained promptly in all seriously injured patients. The presence of blood indicates some injury; however, the degree of hematuria is not necessarily indicative of the degree of damage. Most urinary injuries can be treated conservatively, but rupture of the ureter, bladder, and urethra require early initial repair to prevent urine extravasation.

Neurological Damage.—Peripheral nerve function should be determined in the examination of any wound of the extremities. Simple tests for detection of nerve injuries in both the upper and lower extremities are well known, and detection is relatively easy. The discovery of a peripheral nerve lesion after manipulation is disturbing and requires immediate reinvestigation.

The state of consciousness frequently alters the extent and interpretation of the complete examination. It masks symptoms of serious injury and causes delay in the management of injuries otherwise easy to care for.

Orthopedic Problems.—Most traumatic lesions alone do not present a serious therapeutic problem, but, when encountered in combination with other things, they create a major surgical problem. An open reduction may be advisable when it is the only injury, but in multiple injuries it may be contraindicated. Débridement of open wounds, reduction and immobilization of fractures, early amputation of all devitalized parts, and other procedures all play a major part in the rehabilitation of the extensively injured patient. Early grafting or suturing of major blood vessels by those specialized in the field may be much more important as the immediate operation than fixing the fracture properly.

The prevention of infection should not be left out of an orthopedic surgeon's thoughts in managing his injured patient. The use of a broad-spectrum antibiotic and whole blood, débridement of devitalized tissue, and the use of prophylactic antitetanic serum and toxoid therapy are all essential.

Summary

In management of a patient with multiple injuries, efforts should be directed first toward relieving the causes of asphyxia and then to treatment of sucking chest wounds, maintenance of a free airway, arrest of hemorrhage and replacement of blood, splinting of fracture, and, finally, débride-

ment of the contaminated wounds. During the time a patient is unconscious on a stretcher, no harm can come from carefully and simply splinting all extremities. Every physician who treats severely injured patients must be prepared to institute emergency lifesaving measures in any part of the body. He may not do as well as the specialist, but he can often do a tracheotomy and aspirate mucus and blood from the nose and throat, stop sucking chest wounds, give intravenous fluids and blood, and adequately splint badly mangled extremities.

The judicious performance of amputation of a badly mangled extremity can also make the difference between returning a patient soon after injury to an active useful life and condemning him to prolonged invalidism.

266 Beacon St.

MANAGEMENT OF THE SEVERELY INJURED PATIENT—GENITOURINARY ASPECTS

John W. Schulte, M.D., San Francisco

A carefully considered, systematic, orderly approach is essential when one is dealing with possible injury to the genitourinary tract. Three fundamental steps are involved: history of injury, physical findings, and laboratory studies.

Fundamental Steps in Diagnosis

History.—A careful history is all important. If the patient is unconscious, or unable to give an accurate account of his injury, a witness to the accident should be questioned.

Different varieties of trauma can be expected to cause specific lesions in the genitourinary tract. For example, a person working on a roof who falls astride a scaffold is most likely to rupture the bulb of the urethra. Someone who suffers a severe blow directly over a distended bladder is likely to suffer an intraperitoneal rupture of the bladder; a person who sustains a compression fracture of the pelvis is apt to have an extraperitoneal rupture. A blow over the angles of the 11th and 12th ribs is more likely to cause a ruptured kidney than ruptured urethra.

Physical Findings.—A thorough physical examination is mandatory and should include a rectal examination. To limit one's field of vision to just the possibility of a ruptured bladder would be shortsighted when the patient's immediate problem is anoxia and paradoxial breathing due to a crushed chest.

Rectal examination may demonstrate that the prostate gland lies in the middle of the pelvis rather than its normal position, which suggests complete rupture of the prostatomembranous urethra.

From the Department of Surgery (Urology), University of California School of Medicine.

Read in the Panel Discussion on Management of the Severely Injured Patient before the General Scientific Meeting at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23, 1958.

History of injury, physical findings, and laboratory studies are the three fundamental steps in the diagnosis of any urologic injury. To limit one's field of vision to just the possibility of a ruptured bladder would be shortsighted when the patient's immediate problem is anoxia and paradoxial breathing due to a crushed chest. The prognosis of anterior and posterior urethral trauma must be a guarded one. Dense strictures may result from these injuries, requiring periodic urethral dilatation for months or years. Immediate surgical treatment is indicated in rupture of the bladder after the patient has been suitably prepared. Shock must be treated first by whatever method is most appropriate. The common cause of ruptured kidney is a direct blow to the loin over the region of the 11th and 12th ribs. Follow-up observations should be made on patients who have sustained a ruptured kidney. A kidney may be injured sufficiently to cause its ultimate death, yet not sufficiently to warrant immediate operation. Such damage may be found only by repeat studies several months later.

Laboratory Studies.—Laboratory studies are dictated by the patient's needs and should include blood cell count and hematocrit value determination, urinary studies with microscopic examination of the urinary sediment, and roentgenograms for skeletal and soft tissue injuries. Special roentgeno-

graphic examinations, such as the excretory urogram, retrograde cystogram, and urethrogram, are indispensable aids to diagnosis.

This discussion will be limited to diagnosis and treatment of the common types of genitourinary injuries—ruptures of the urethra, bladder, and kidney.

Ruptured Urethra

Ruptures of the urethra may be divided into two groups: (1) those occurring distal to the triangular ligament and (2) those proximal to it. The latter are further subdivided for purposes of treatment into complete and incomplete ruptures.

Anterior Urethral Injuries.—Ruptures distal to the triangular ligament are caused by direct, external trauma and usually occur at or near the bulb of urethra. A common type is the so-called straddle injury.

A blow to the perineum followed by bleeding from the urethral meatus, initial hematuria, or inability to void is the common history. If the rupture has been complete and the patient attempts to urinate, he may complain of pain and sudden increased swelling of the perineum and scrotum. These symptoms indicate urinary extravasation.

The most important positive physical finding associated with rupture of the anterior urethra is blood at the urethral meatus. Further examination reveals ecchymosis and edema of the scrotum and perineum. If urinary extravasation has occurred, the tissues are tense and distended from the urogenital perineum forward and edema may extend upward into the subcutaneous tissues of the anterior abdominal wall. Rectal examination demonstrates the prostate to be in normal position. If the patient has urinary extravasation, he may be acutely ill; rapid pulse and hypotension may be noted. In the absence of urinary extravasation, the patient, while complaining of pain, does not appear particularly ill.

A roentgenogram of the pelvis should be obtained to determine skeletal injury. This accomplished, the patient remains on the x-ray table and urologic studies are done. An urethrogram is obtained first. My practice is to mix K-Y lubricating jelly (containing boric acid, glycerol, chondrus, and tragacanth) with an equal part of a 25% methiodal (Skiodan) sodium solution for contrast medium; the mixture is gently instilled into the urethra with a bulb syringe, and anteroposterior and oblique roentgenograms are made. From these studies the site and degree of injury can be determined.

If the roentgenographic studies demonstrate an incomplete rupture, an attempt is made to pass an urethral catheter into the bladder. If this is successful, the catheter is left indwelling for three to five weeks.

If the films show a complete urethral rupture, or if a catheter cannot be inserted past the area of incomplete tear, immediate surgical treatment is indicated. The type of operation undertaken depends on the skill and training of the surgeon.

If there is any question in the surgeon's mind concerning his ability to deal with such a problem directly, the simplest and most expedient operation to perform is a suprapubic cystostomy. This procedure diverts the urine and obviates the possibility of urinary extravasation. Secondary repair of the urethral injury can be done later. If the surgeon feels capable of attempting primary repair, he should proceed at once.

If subcutaneous urinary extravasation has occurred at the time of or subsequent to the injury, adequate drainage of perineum and scrotum should be established. The urethra is a contaminated field, and organisms washed into the surrounding tissues by urine grow luxuriantly; a rapidly progressing phlegmonous type of infection may ensue which may soon be fatal.

Posterior Urethral Injuries.—Rupture of the prostatomembranous urethra results from a shearing type of force and is most often associated with severe trauma to the bony pelvis.

The history is usually of a direct blow to the pelvis, such as may occur in heavy industry or an automobile-pedestrian accident.

Positive urologic history consists of the patient being unable to void or having voided a small amount of grossly bloody urine. Abdominal pain is not specific because of the usually associated pelvic, skeletal injury.

In regard to physical findings, the presence of purplish discoloration above the symphysis pubis, with associated lower abdominal tenderness and spasm, suggests possible rupture of the posterior urethra. The most important physical finding is obtained from rectal examination. If there is complete division of the prostatomembranous urethra, the prostate will be felt to be high in the pelvis rather than in its normal position. Because of extravasation of blood and urine in incomplete rupture, the boundaries of the prostate may be indefinite.

Since such patients usually have multiple injuries and may be critically ill, they should be disturbed as little as possible; all ancillary diagnostic studies should be made at one time as soon as the patient's condition permits.

When the history and physical findings suggest rupture of the posterior urethra, an urethrogram made as previously described will demonstrate the site and extent of injury. An incomplete rupture will allow some of the contrast medium to enter the bladder and some to be extravasated. A complete rupture allows most of the contrast medium to extravasate around the bladder and prostate; the latter is seen to be elevated in the pelvis.

An alternative procedure is to pass an urethral catheter and perform retrograde cystography, with use of a 25% solution of methiodal. This is the usual method, since it may be difficult to determine by history and physical findings alone whether the bladder or posterior urethra is ruptured. When retrograde cystography is used, the catheter may be seen to lie outside the bladder in complete rupture of the urethra with perivesical extravasation of contrast medium. In incomplete rupture, the bladder may be seen to be elongated and compressed by perivesical collection of blood and urine with a leak at the site of injury.

In treatment, urethral continuity is reestablished and the pelvic retroperitoneum is drained. The techniqne used depends on the surgeon's judgment.

Prognosis.—The prognosis of anterior and posterior urethral trauma must be a guarded one. Dense strictures may result from these injuries, requiring periodic urethral dilatation for months or years. Loss of sexual potency, particularly with posterior urethral injuries, is common and may be permanent.

Ruptured Bladder

Rupture of the bladder is either intraperitoneal or extraperitoneal. The history of injury gives an important clue as to which form of rupture may be present.

Intraperitoneal Rupture.—A direct blow over the suprapubic area is most likely to cause an intraperitoneal rupture of the bladder. This is particularly true if the patient has a full bladder at the time of injury. Trauma is followed by severe suprapubic and lower abdominal pain and passage of bloody or smoky urine.

These patients may be in shock. The abdomen is tense, particularly in the lower quadrants, and board-like rigidity may be noted immediately after injury. Peristalsis is absent or hypoactive. Rectal examination may define a fluctuant area in the region of the cul-de-sac.

Laboratory findings reveal the urine to be usually grossly bloody or smoky. It occasionally may appear relatively clear, but microscopic hematuria is always present.

Retrograde cystography is diagnostic. Three films are made: a preliminary roentgenogram, a film with the bladder distended with a 25% solution of methiodal, and one after the bladder has been evacuated. It is important that the bladder be filled to capacity; a small tear may be sealed immediately by omentum and so not be visible otherwise on the roentgenogram.

The postevacuation roentgenogram is particularly important, because it shows contrast medium extravasated into the peritoneal cavity or pooled in the cul-de-sac.

Extraperitoneal Rupture.—The extraperitoneal rupture is most often associated with fractures of the pelvis and results from indirect trauma to the bladder.

The history is almost identical to that obtained in the intraperitoneal rupture, except for the type of trauma. A crushing type of pelvic injury is the usual story.

Physical findings are usually similar to those seen in patients with intraperitoneal rupture, with few exceptions. Among these are more localization of pain and spasm to the lower quadrants, a bluish discoloration of the suprapubic skin, and normal rectal findings.

Urinary studies also will give results similar to those found in patients with intraperitoneal rupture. Plain roentgenograms usually show deformities of the pelvic skeleton, varying from multiple fractures to separation of the symphysis pubis or sacroiliac joints.

Retrograde cystography done in the same manner as in intraperitoneal rupture shows perivesical extravasation of radiopaque fluid in the evacuation roentgenogram.

Treatment.—Immediate surgical treatment is indicated in both types of rupture of the bladder after the patient has been suitably prepared. Shock must be treated first by whatever method is most appropriate. Other injuries, if more pressing, are treated before urologic surgical repair is undertaken.

In both intraperitoneal and extraperitoneal ruptures of the bladder, abdominal exploration is mandatory. It is imperative that the peritoneal cavity be opened and the pelvic viscera, including small intestine and rectum, be examined; a force strong enough to cause rupture of the urinary bladder may also cause severe injury to adjacent organs. Injuries to other organs are treated first.

Treatment of intraperitoneal rupture of the bladder consists of mobilization of the rent in the peritoneum from the surface of the bladder, closure of the bladder mucosa and muscle, and reapproximation of the peritoneum. After this, urinary drainage is established suprapubically by means of cystostomy. Dependence on an indwelling urethral catheter alone is not recommended, since the lumen may become occluded, the bladder may become distended, and a leak may occur at the site of repair.

Treatment of extraperitoneal rupture of the bladder again consists first in exploration of the peritoneal cavity. If no associated lesions are present, the peritoneum is closed and the bladder is exposed extraperitoneally, the prevesical space being widely opened on either side. This permits drainage of the extravasated urine and blood. The bladder is then entered suprapubically, and a cystostomy drain is inserted. No attempt is made to identify the site of rupture unless it easily comes to view. Experience has shown that lacerations of the bladder will heal without suture if the bladder is put at rest by cystostomy drainage.

The prevesical space is drained for 10 days, at which time cystotomy tube and drains may be removed and the cystotomy allowed to close spontaneously or encouraged by means of urethral catheter drainage.

Ruptured Kidney

Because of its anatomic position and coverings, the kidney is not prone to injury. There are, however, predisposing causes for rupture of the kidney, the most common of which is hydronephrosis. The common cause of ruptured kidney is a direct blow to the loin over the region of the 11th and 12th ribs.

History and Findings.—The pertinent history is of a direct blow to the loin followed by pain in the affected side and the passage of grossly bloody urine, sometimes with blood clots. The pain is severe and may radiate anteriorly into the abdomen or groin.

The patient may appear acutely ill, pale, and perspiring and have rapid pulse and hypotension. Local physical findings demonstrate spasm of the flank musculature on the injured side with reflex guarding and spasm on the abdominal muscles. An area of ecchymosis may be noted over the loin.

On careful examination a mass in the flank may be felt. If a mass is found, its margins should be marked with ink on the patient's skin for future reference. If the urinary collecting system has been damaged, cutaneous edema may be seen over the area of the lumbar triangle from extravasation of urine.

The urinary specimen is almost always grossly bloody, and red blood cells are always seen microscopically.

A roentgenogram of the abdomen may show injury to the skeleton, including fractures of the ribs or transverse processes. Of diagnostic value is the absence of a psoas shadow on the affected side and the absence or haziness of renal outline.

The most useful diagnostic study used in proving ruptured kidney is the excretory urogram. Contrary to the beliefs of some, excellent studies of the upper and midurinary tracts may be obtained without the usual preliminaries of dehydration and catharsis.

Excretory urograms in the case of a presumably ruptured kidney should be done to obtain the following information: 1. The size, structure, and function of the unaffected kidney. A congenital, solitary kidney is not an uncommon anomaly, and congenital hypoplasia is not rare. It is obvious that a contemplated nephrectomy in the case of renal rupture must be predicated on the presence of a life-sustaining remaining kidney. 2. The degree of injury to the kidney itself. If there has been complete transection of the renal pedicle, contrast medium will not concentrate in the kidney. If the renal substance has been lacerated, intrarenal extravasation will be seen. 3. Injury to the collecting system. If the pelvis or ureter has been torn, extrarenal extravasation will be apparent.

Treatment.—Treatment is initially directed for the patient as a whole. He must be relieved of pain and given such supportive therapy as is necessary to overcome shock if present. Ninety per cent of patients with ruptured kidney require supportive therapy only. The type of operation in the remaining 10% depends on the type and severity of the injury. Surgical intervention should not be considered as long as the patient's general condition improves with supportive treatment. Ominous signs include continued shock in spite of supportive measures or increasing size of a mass in the flank, as demonstrated by repeated physical examination. Either indicates continuing hemorrhage.

If the patient continues to be in shock in spite of transfusion and ancillary treatment, immediate operation is indicated as a lifesaving measure. In my experience with such patients, either the kidney is completely shattered or its vascular pedicle is completely transected. Under these circumstances nephrectomy is usually the operation of choice, depending, of course, on the presence of a second, life-sustaining kidney.

Urinary extravasation demonstrated by excretory urography demands surgical drainage, but this is not urgent and can be done when the patient has recovered from the initial effects of injury. Drainage can easily be established by introducing a Penrose drain through Petit's triangle deep to Gerota's capsule.

Follow-up observations should be made on patients who have sustained a ruptured kidney. A kidney may be injured sufficiently to cause its ultimate death yet not sufficiently to warrant immediate operation. Such damage may be found only by repeat studies several months later.

384 Post St.

ANILERIDINE HYDROCHLORIDE—ITS CLINICAL USE AS AN ANALGESIC AND SEDATIVE

PRELIMINARY REPORT

Robert C. Therien, M.D., Leroy W. Lee, M.D., Edward M. Malashock, M.D.
and
Neal B. Davis, M.D., Omaha

The clinical effects of anileridine hydrochloride have been observed after more than 2,500 administrations to more than 600 patients. It was used both as premedication for general anesthesia in surgery (in doses averaging 50 mg. orally or subcutaneously) and as a postoperative sedative and analgesic (in doses ranging from 25 to 75 mg.). Its effects resemble those of morphine and meperidine, but euphoria was uncommon, and no evidence of addiction was seen even in a patient who received 552 doses during the course of metastatic carcinoma of the colon. In patients who received the drug daily for various periods of time, there was no evidence of withdrawal symptoms when a series of administrations was interrupted. Nausea occurred in eight and emesis in six instances. Respiratory depression caused by excessive doses in a few patients was easily counteracted by levallorphan in doses of 1 mg. for every 25 mg. of anileridine hydrochloride. It was effective in the very old as well as the very young and showed promise of usefulness in a wide diversity of medical and surgical situations.

Anileridine hydrochloride is a substituted meperidine which is chemically known as ethyl-1-(4-aminophenethyl)-4-phenylisonipecotate dihydrochloride. The structure is shown in the figure. Experimental observations in animals and man have proved it to be a potent analgesic agent with high activity and relatively mild side-effects when given orally. In animals, the compound approaches the analgesic potency of morphine and is more potent than meperidine. It has a prompt onset of action (15 to 30 minutes) and a long duration of analgesia (five to six hours). The side-reactions, such as general depression, depression of respiration, and lowering of blood pressure, are considerably milder than those produced by morphine and somewhat milder than those of meperidine.

Synthesis of the compound was accomplished in 1956 by Weijlard and co-workers.[1] Pharmacological characteristics of anileridine were studied by Orahovats and associates,[2] who found aside from the characteristics already enumerated that the compound had an antitussive effect, an anticholinergic effect, and an antihistaminic effect. It did not produce constipation, as was seen with morphine. It was well tolerated by mice, rats, cats, and dogs in single and repeated administrations. Tolerance to the analgesic effect developed slower for anileridine than for either morphine or meperidine. Local tissue injection with 50 mg. of anileridine produced considerably less reaction than similar solutions of meperidine. The effects of anileridine were reversed by nalorphine (Nalline) hydrochloride.

Porter [3] described the absorption and metabolism of anileridine and suggested analytical methods for identifying anileridine in the tissues and body fluids. He stated that the metabolism and excretion of anileridine are similar to those of meperidine. The highest concentrations of anileridine were found in the lungs, kidneys, and brain. Major excretion was by way of the kidneys.

Observations on the effects of anileridine in man have been reported by Keats and co-workers,[4] Dripps and co-workers,[5] Wallenstein and Houde,[6] and Stage.[7]

From the departments of anesthesiology and urology, Bishop Clarkson Memorial Hospital, and the University of Nebraska College of Medicine.

Read before the Section on Anesthesiology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Observations on Drug Usage and Effect

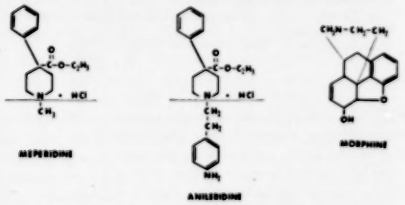
Our observations were begun shortly after the compound was synthesized in 1956 and proved to be suitable for administration to animals and man, and they have continued to this time. During this time we have given anileridine to over 600 patients. We have used various preparations of the drug and various methods of administration. These preparations have included tablet and elixir for oral administration, as well as solution for intramuscular, subcutaneous, and intravenous use. The drug was used for preoperative analgesia and sedation, as well as for postoperative analgesia. Observations for preoperative sedation were made personally by us. The postoperative analgesic effectiveness and durations were observed by special and regular duty nurses. These in turn were reported to the house staff physicians for evaluation. Patients with ad-

vanced painful carcinoma, as well as those with other painful clinical conditions, were observed for its analgesic effect.

In the entire study, anileridine was administered over 1,900 times. For preoperative medication it was given alone in 260 instances, with orally given vinbarbital (Delvinal) sodium, 100 mg., 302 times, and with atropine or scopolamine hydrobromide 70 times—making a total of 632 preoperative administrations. Doses varied from 25 to 100 mg., but the average subcutaneous and oral dose was 50 mg. For postoperative sedation and analgesia, anileridine was given 1,320 times. The dose ranged from 25 to 100 mg. The average doses were 50 to 75 mg.

In this series of 632 patients coming to surgery and receiving anileridine preoperatively, regional anesthetics were used in 562 and general anesthetics in 70 instances. The types of surgical procedures were as follows: cystoscopy (71), cystoscopy, ureteral catheterization, or manipulation (321), renal operations (24), ureteral operations (23), perineal prostatectomy (38), transurethral prostatectomy (61), suprapubic prostatectomy (4), suprapubic vesical operation (11), transurethral resection of bladder tumor (22), scrotal operation (70), bilateral adrenalectomy, retroperitoneal tumor (3), urethral or penile operation (23), presacral oxygen study (4), breast biopsy (2), and gynecologic surgery (59).

Inasmuch as several of these patients had two separate surgical procedures performed during the same hospitalization, it offered a novel way to observe the comparative effect of meperidine and anileridine preoperatively in the same patient. A group of 50 patients were given anileridine subcutaneously with orally given vinbarbital sodium on one occasion, and an equal dose of meperidine was substituted for anileridine on another. All medication in this series was given one hour preoperatively. Since the operative procedure in these patients was done with use of regional anesthesia, it was possible to observe them very accurately in the operating room and recovery room for a minimum of two hours. It was found that, in this series, 50 mg. of anileridine was as effective as 75 mg. of meperidine for comparable signs of analgesia and sedation.



Structural formulas for meperidine, anileridine, and morphine.

In patients receiving anileridine, the onset of analgesia appeared in 15 to 30 minutes and was profound at 60 minutes. The analgesic effect of anileridine appeared to last for one to seven hours, with an average of three to four hours. These observations were made with average dosages of 50 to 75 mg. No deaths or severe toxic reactions were seen incident to administration of anileridine. Overdoses in a very few patients were manifested by respiratory depression. The respiratory depression was easily counteracted by administration of levallorphan in a ratio of 25:1 for the unanesthetized patient. When intravenously given barbiturates were used with a general anesthetic, the antagonist dose was doubled, i. e., 12.5 mg. of anileridine was counteracted by 1.0 mg. of levallorphan.

TABLE 1.—*Case and Dosage Data in Patients Receiving Anileridine*

Case, No.	Sex	Age, Yr.	Dosage Data: No.	Dosage Data: Size, Mg.	Dosage Data: Interval, Days
1	F	74	66	50	20
2	F	21	35	50	9
3	M	70	31	25	21
4	F	22	28	50	8
5	M	74	23	50	15
6	M	59	27	75	30
7	M	33	47		8, 9*

* Patient received 23 doses in eight-day period and, on second admission two months later, 21 doses in nine-day period for second operative procedure.

Untoward effects observed were as follows: nausea (eight), emesis (six), vertigo (two), headache (two), sensation of choking (one), itching (one), and deep sedation (three). The latter effect occurred in patients receiving 75 mg., 100 mg., and 100 mg. respectively. No evidence of abdominal cramps or constipation was seen. Neither evidence of toxic psychotic effects nor severe circulatory depression was seen. Euphoria was uncommon.

Special Uses and Addiction

Special Uses.—Observations on special uses of anileridine were made as follows. In children, anileridine used both preoperatively and postoperatively appeared to be effective and well tolerated. The dosage given was one-half the standard accepted meperidine dosage for age and weight. The pain of ureteral colic, urinary and gallbladder spasm, and coronary thrombosis, peripheral vascular pain, and pain of metastatic carcinoma was relieved. In the geriatric age group, anileridine was effective preoperatively and postoperatively, as well as in other painful conditions. There were 170 patients over 80 years of age in this group. It did not produce the psychic disorientation so often seen with morphine when used in aged persons. The large percentage of geriatric-patient surgical procedures done is shown in the previous section. In the series were 12 severe diabetic patients and 5 with severe asthma. In both groups, the severe disease was not aggravated and the drug appeared to

be well tolerated. Dripps and associates [5] have demonstrated the antihistaminic effect of anileridine in man. The severe tremor of Parkinsonism was noted to disappear in two patients after administration of anileridine.

Addiction.—We have found anileridine to produce no evidence of addiction. Our series includes several patients who received a considerable number of repeated doses with subsequent easy withdrawal of the drug. Table 1 shows dosage regimen of our patients receiving the drug hypodermically in multiple doses.

Orally, for metastatic disease, four patients received repeated doses as shown in table 2. In the patient in case 2 (table 2), medication was withheld 10 days during the middle of the series without evidence of withdrawal symptoms. A total of 105 patients received oral medication with anileridine. In all, this medication was well tolerated.

TABLE 2.—*Case and Dosage Data in Patients Receiving Anileridine for Metastatic Disease*

Case, No.	Carcinoma of	Dosage Data		
		No.	Size, Mg.	Interval, Days
1	Kidney	66	25-50	20
2	Bladder	100	25-50	30
3	Bladder	232	25-50	180
4	Colon	502	25-50	128

The oral route of medication for drugs is considered much less likely to cause addiction. The hypodermic route, for psychological reasons, is considered more likely to cause addiction in the person requiring continual narcotic medication. According to some psychiatrists,[8] the hypodermic route provides a symbolic accentuation of the importance of the medicine. For this reason, anileridine with its high oral effectiveness can be considered a very useful addition to the group of orally effective drugs used for the relief of pain.

Summary

The clinical use of anileridine as a preoperative and postoperative analgesic and sedative was observed in a study of over 600 patients. This study showed anileridine to be a valuable addition to the present group of analgesic-sedative agents. It is effective given orally and parenterally, with a minimal amount of undesirable side-effects. Anileridine was found to be effective and well tolerated by children, as well as by patients of advanced age.

Further observations should be continued of the effects of anileridine in the management of patients with severely painful clinical conditions, such as ureteral colic, biliary colic, embolism, and coronary thrombosis. Its effects on patients with diabetes, asthma, and Parkinsonism should also be observed further.

Addendum

Since the completion of this study series, an additional 653 doses of anileridine have been administered, without any remarkable change from our previous study's statistics.

800 Doctor's Bldg. (Dr. Therien).

The anileridine used in this study was supplied as Leritine by Merck Sharp & Dohme Division of Merck & Co., Inc., Philadelphia.

References

1. Weijlard, J., and others: New Synthetic Analgesic, J. Am. Chem. Soc. **78**:2342-2343 (May 20) 1956.

2. Orahovats, P. D.; Lehman, E. G.; and Chapin, E. W.: Pharmacology of Ethyl-1-(4-Aminophenethyl)-4-Phenylisonipecotate, Anileridine, New Potent Synthetic Analgesic, J. Pharmacol. & Exper. Therap. **119**:26-34 (Jan.) 1957.

3. Porter, C. C.: Absorption and Metabolism of Anileridine, Ethyl-1-(4-Aminophenethyl)-4-Phenylisonipecotate, J. Pharmacol. & Exper. Therap. **120**:447-451 (Aug.) 1957.

4. Keats, A. S.; Telford, J.; and Kurosu, Y.: Studies of Analgesic Drugs: Anileridine Dihydrochloride, Anesthesiology **18**:690-697 (Sept.-Oct.) 1957.

5. Dripps, R. D.; Millar, R. A.; and Kneale, D. H.: Comparison of Anileridine, Morphine and Meperidine in Man, Surg. Gynec. & Obst. **105**:322-326 (Sept.) 1957.

6. Wallenstein, S. L., and Houde, R. W.: Clinical Evaluation of Relative Analgesic Potencies of Anileridine, Meperidine and Morphine, abstracted, J. Pharmacol. & Exper. Therap. **122**:81 (Jan.) 1958.

7. Stage, J. T.: Anileridine as Anesthetic Agent, J. Florida M. A. **44**:143-145 (Aug.) 1957.

8. Faucett, R. L.: Drug Addiction and Other Considerations in Management of Pain with Narcotic Drugs, Proc. Staff Meet. Mayo Clin. **32**:45-54 (Feb. 6) 1957.

ROENTGENOLOGIC EVIDENCE OF FETAL DEATH.—At roentgen examination of relatively mature fetuses before delivery, a zone of reduced density is usually discovered around the head of the fetus, produced by the subcutaneous layer of fat. If the fetus is dead, this transparent zone in certain cases is separated from the cranium by a layer of the same density as the other soft tissues of the fetus. This finding was described for the first time by Deuel in 1947 as a sign of intrauterine fetal death. Intrauterine fetal death can be determined in the majority of cases (more than 75 per cent) by means of a roentgenologic examination. Free gas is the most common and the most important sign of fetal death. In cases where the death of the fetus occurs when the fetus is almost at term, free gas and Deuel's halo sign are frequently noted, whereas when the fetus dies in an early stage of development, the most common roentgenologic sign of death is the maceration of the trunk. —O. F. Holm, Deuel's Halo Sign, *The American Journal of Roentgenology*, October, 1958.

THE PROBLEM OF CARDIAC ARREST

Kenneth C. McCarthy, M.D., Toledo, Ohio

Cardiac arrest is best defined as sudden cessation of cardiac function from the effects of anesthesia or surgical manipulation. The incidence of cardiac arrest has been recorded as anywhere from 1 per 696 to 1 per 24,000 operations. The natural tendency to evade responsibility by reporting deaths due to anesthesia as due to cardiac arrest must not be overlooked. The patient should be protected against noxious reflexes by proper and adequate premedication. Hypoventilation with its vicious offspring, hypoxia and hypercapnia, must be avoided. All exponents of the art of anesthesiology must be diligent and conscientious in preventing this tragedy.

The Chairman of the Section on Anesthesiology traditionally reviews the growth of the specialty from the date of Adam's historic thoracoplasty. Recent advances in research and technique may be viewed proudly, and certain innovations may be regarded as radical and therefore dangerous practices. However, a new day is certainly dawning; we are on the threshold of a new and glorious era in anesthesiology.

I am also in the happy position of knowing that this paper will have an assured if not attentive audience. This is too good a chance to pass up, and it gives an opportunity to discuss a problem that is assuming increasing importance in anesthesia and surgery. This subject is cardiac arrest.

This topic is attracting more and more interest. A superficial review of the literature shows six times as many papers published in the last 5 years as in the previous 50. Most of these authors believe that the incidence is increasing, but no one agrees as to what this incidence actually is. Some typical figures are as follows: Natof and Sadove [1] record the incidence of cardiac arrest as 1 per 696 operations, Lahey and Ruzicka [2] as 1 per 1,000, Hingson and co-workers [3] as 1 per 1,078, Briggs and associates [4] as 1 per 1,400, Jacoby and associates [5] as 1 per 1,588, Bergner [6] as 1 per 2,000, Johnson and Kirby [7] as 1 per 3,600, Bonica [8] as 1 per 4,150, Merritt and Osterhagen [9] as 1 per 8,600, and Blades [10] as 1 per 24,000.

This great disparity in figures must indicate that everyone does not mean the same thing by cardiac arrest. One of the greatest difficulties is to know what we are talking about. To describe this entity, Natof and Sadove [1] list 12 separate and different definitions. Of these definitions, that of Blades [10] is simple and logical: "sudden cessation of cardiac function from the effects of anesthesia or surgical manipulation." If this definition were followed, many cases would be eliminated that are now called cardiac arrest and the subject could be viewed in its true perspective. Some surgeons apply the term to every patient who dies in the operating room and who is not completely exsanguinated. Obviously, every death from any cause could be called cardiac arrest, for that is the final episode in every fatality. Actually, a careful analysis of operating room deaths shows that roughly half are due to surgical accidents, shock, or primary disease and should not be termed as due to cardiac arrest.[11]

Anesthetist, Flower and Mercy hospitals.

Chairman's address, read before the Section on Anesthesiology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

These reviews also throw doubt on the widely held theory that there is an alarming increase in the incidence of this condition. For example, at Flower Hospital, Toledo, Ohio, the operative mortality has shown a steady reduction from 1.9% in the 1930's to 1.6% in the 1950's in spite of an increase in major pulmonary and cardiovascular surgery. Certainly there has been no increase in cardiac arrest or even operating room deaths. The apparent increase must be due to a greater awareness of the problem, so that more cases are recognized and reported. We must not overlook the natural tendency to evade responsibility by saying that a death due to anesthesia is due to cardiac arrest. The latter, for which no cause is known, is obviously an act of God for which human error cannot be held accountable.

Cardiac arrest has been defined as total circulatory failure for which no cause is apparent.[4] However, in every case there is a causative factor, and the reason that it is not apparent must be because we did not look for it or ignored it if present.

Causes

Hypoxia.—Oxygen lack has a twofold effect on the heart. Central nervous system depression causes respiratory and vasomotor failure with resulting cardiac hypoxia. There is also a direct effect on the myocardium, which, unlike skeletal muscle, cannot rest to restore oxygen debt. Even short periods of suboxygenation may produce cardiac standstill. Lactic acid, the normal product of muscular activity, increases with hypoxia. With a concentration of only 0.07% it will produce cardiac

arrest, whereas skeletal muscle will function even though the concentration is threefold. Cardiac hypoxia is produced by any factor that interferes with coronary circulation, as well as a frank low oxygen intake. This cardiac ischemia establishes a trigger zone that acts as a focus for ventricular fibrillation. Types of hypoxia and their causes include (1) anoxic, due to respiratory obstruction, low inspiratory oxygen level, or hypoventilation; (2) anemic, due to hemorrhage or anemia; (3) stagnant, due to shock, cardiac inefficiency, hypotensive drugs, or spinal anesthesia; (4) histotoxic, due to overdosage of anesthetics; and (5) metabolic, due to high oxygen demand. Hypoxia is frequently associated with, and made more dangerous by, hypercapnia.

Parasympathetic Stimulation.—Though formerly there has been skepticism regarding the vagus reflex, some reports seem to establish beyond reasonable doubt that tracheal, laryngeal, hilar, ocular, and mesenteric stimulation can produce cardiac inhibition by initiating vagus reflexes. A number of factors and agents potentiate this action. Hypoxia, hypercapnia, barbiturates, and cyclopropane are common causes.

Neostigmine is used freely as an antagonist to tubocurarine and other relaxants with similar action. It is important to remember that, unless the vagus is adequately depressed by atropine, this drug produces powerful stimulation which can (and has) initiated cardiac arrest.

Sympathetic Stimulation.—Guedel postulated that ventricular fibrillation could be produced by epinephrine released by emotional trauma incident to the induction of anesthesia.[12] The high incidence of cardiac arrest during induction lends support to this theory. Of course the danger of administering epinephrine or posterior pituitary injection (Pituitrin) in conjunction with cyclopropane anesthesia is well known. Ventricular fibrillation is to be anticipated. The preoperative preparation of the patient with adequate sedation is still vital. A recent tendency to belittle the euphoric effects of morphine is ill founded.[13] Several million narcotic addicts testify that morphine produces psychic effects that cannot be obtained with other sedative drugs.

Overdosage.—An overdose of practically any anesthetic agent will produce cardiac irregularities, vasomotor depression, and asystole. Doubtless some of this effect is hypoxic in nature, but many agents have a direct effect on the heart muscle or its conduction mechanism. The role of chloroform and ethyl chloride is well recognized. The other recently popular halogen anesthetics, trichloroethylene (Trilene) and halothane (Fluothane), seem to have similar properties, and great caution must be observed when using these drugs, for reports of cardiac arrest after their use are becoming common.[14] It is easy to give an overdose of any agent to a patient when, as is common, assisted or controlled respiration is being used.

Under normal circumstances overdose produces respiratory depression which by reducing ventilation tends to limit the amount of gas inhaled. However, when hyperventilation is artificially induced, an excess can be pumped into the circulation without the ordinary signs of deep anesthesia being present. The result is hypoxia from vasomotor depression and asystole from direct myocardial paralysis.

Trauma.—The heart may be directly embarrassed during intrathoracic surgery. This is undoubtedly a cause of the high incidence of cardiac arrest during these operations. There may be pressure on the auricles or great vessels preventing adequate filling. Wiggers describes also the onset of ventricular fibrillation by direct injury to the heart. This may be produced by external trauma as well as by direct interference with cardiac action.

Other Causes.—Less common causes of cardiac arrest to be mentioned in passing are artificially induced hypothermia and potassium or procaine intoxication. References to these are also appearing with increasing frequency.

The presence of preexisting cardiac disease, of course, makes the heart more susceptible to arrest from any of these causes. Furthermore, a damaged heart is much more difficult to restart or, restarted, to be maintained permanently with a regular efficient beat.

Diagnosis and Treatment

Diagnosis.—The diagnosis cannot be made without close observation of the patient. No anesthesia can be conducted "in absentia." A careful, conscientious, and competent individual must be in attendance constantly. Every breath must be noted, the pulse should be palpated constantly, and the blood pressure should be checked from minute to minute. An experienced anesthesiologist can often suspect cardiac distress by simple observation of the patient. Irregularities, bradycardia, or sudden hypotension are warning signs. The diagnosis is established not by electrocardiogram, or even auscultation, but by the absence of a palpable pulse in a major vessel. Treatment must be instituted without a moment's delay.

It is hoped that this presentation, by stressing that errors in technique or judgment are responsible for most cardiac arrests, might make discussion of treatment superfluous. One ounce of prevention is still worth many pounds of cure, for even under the best circumstances the results of treatment are

unsatisfactory. The mortality, as quoted by various authors, is as follows: Bergner,[6] 35%; Ruth and coworkers,[15] 40%; Blades,[10] 50%; Lahey and Ruzicka,[2] 62%; Briggs and associates,[4] 63%; Freeman and coworkers,[16] 65%; and Barber and Madden,[17] 66% (average, 54.4%).

These statistics unfortunately do not give any information on one of the most distressing aspects of this subject. Many patients, listed as having recovered from cardiac arrest, undoubtedly are doomed to a hopeless vegetative existence due to cortical damage from cerebral anoxia.

Treatment.—The treatment of cardiac arrest has become well standardized and need not be discussed in detail. Artificial respiration with an adequate airway must be instituted as soon as the diagnosis is even suspected. No time should be wasted in intubation at this time. In many cases of simple hypoxia, reoxygenation will reestablish the heartbeat, but this must not be relied on. The chest must be opened immediately and alternate manual compression and decompression of the heart—not "massage"—instituted. The rate should be as rapid as diastolic filling permits, though most operators become fatigued rapidly if rates above 100 per minute are attempted. One should pause occasionally to see if spontaneous beating is resumed. Blood volume must be rapidly restored by intravenously given fluids and/or blood.

The tone of a flaccid heart may be restored by 1:1,000 epinephrine solution (5 cc.) directly injected. Its tendency to produce ventricular fibrillation must be recognized. Should this occur, electroshock with domestic current or a special defibrillator may stop the irregular contractions and allow massage to restore regular rhythm. Procaine by direct injection, topical application, or intravenous injection is recommended in an effort to overcome fibrillation by decreasing cardiac irritability.

It is difficult to predict a successful result. Patients who are moribund or have preexisting cardiac pathology will respond poorly, if at all. Each case must be individually evaluated before treatment is abandoned. Hosler [18] reported complete recovery after eight hours of continuous cardiac massage.

Successful resuscitation depends on (1) the immediate reestablishment of cardiac and cerebral oxygenation and (2) a more deliberate restoration of the spontaneous heartbeat.

Conclusions

I would make a plea to all exponent's of the art of anesthesiology that they be diligent and conscientious in preventing the tragedy of cardiac arrest. The reputation of this profession and the lives of the patients are at stake. Avoid hypoventilation with its vicious offspring, hypoxia and hypercapnia. Protect the patient against noxious reflexes by proper and adequate premedication. Mistrust the halogens. One agent well understood and administered still is more valuable than a polypharmaceutical barrage, of which the evaluation is difficult. Keep it simple, be watchful, be careful, be safe.

2228 Ashland Ave. (10).

References

1. Natof, H. E., and Sadove, M. S.: Cardiovascular Collapse in Operating Room, Philadelphia, J. B. Lippincott Company, 1958, pp. 5-92.

2. Lahey, F. H., and Ruzicka, E. R.: Experience with Cardiac Arrest, Surg. Gynec. & Obst. **90**:108-118 (Jan.) 1950.

3. Hingson, R. A.; Holden, W. D.; and Barnes, A. C.: Mechanisms Involved in Anesthetic Deaths, New York J. Med. **56**:230-236 (Jan. 15) 1956.

4. Briggs, B. D.; Sheldon, D. B.; and Beecher, H. K.: Cardiac Arrest: Study of 30-Year Period of Operating Room Deaths at Massachusetts General Hospital, 1925-1954, J. A. M. A. **160**:1439-1444 (April 28) 1956.

5. Jacoby, J.; Flory, F. A.; Ziegler, C. H.; and Hamelberg, W.: Safety in Surgery, Anesth. & Analg. **34**:346-363 (Nov.-Dec.) 1955.

6. Bergner, R. P.: Cardiac Arrest: Some Etiological Considerations, Anesthesiology **16**:177-189 (March) 1955.

7. Johnson, J., and Kirby, C. K.: Cardiac Arrest During Pulmonary Resection: Etiologic Factors and Management, Am. J. Surg. **89**:56-63 (Jan.) 1955.

8. Bonica, J. J.: Cardiac Arrest, Northwest Med. **52**:719-723 (Sept.) 1953.

9. Merritt, H. E., and Osterhagen, H. F.: Cardiac Arrest and Its Management in Rural Area Hospitals, J. Michigan M. Soc. **54**:72-75 (Jan.) 1955.

10. Blades, B.: Cardiac Arrest, J. A. M. A. **155**:709-712 (June 19) 1954.

11. References 4 and 5.

12. Harvey, W. P., and Levine, A.: Paroxysmal Ventricular Tachycardia due to Emotion: Possible Mechanism of Death from Fright, J. A. M. A. **150**:479-480 (Oct. 4) 1952.

13. Beecher, H. K.: Preanesthetic Medication, editorial, J. A. M. A. **157**:242-243 (Jan. 15) 1955.

14. Chang, J.; McCartney, H. H.; and Graves, H. B.: Clinical Experience with Fluothane, New Non-explosive Anaesthetic Agent, Canad. Anaesth. Soc. J. **4**:187-206 (July) 1957. Hudon, F.; Jacques, A.; Clavet, M.; and Houde, J.: Clinical Observations on Fluothane Anaesthesia, ibid. **4**:207-234 (July) 1957. Stephen, C. R., and others: Evaluation of Fluothane for Clinical Anaesthesia, ibid. **4**:246-258 (July) 1957.

15. Ruth, H. S.; Buckley, M. L.; and Keown, K. K.: Cardiac Asystole, J. A. M. A. **164**:831-835 (June) 1957.

16. Freeman, R. V.; Berger, L. M.; Cohen, S.; and Sells, W. A.: Major Neurological Residuals Following Resuscitation for Cardiac Arrest, J. A. M. A. **155**:107-109 (May 8) 1954.

17. Barber, R. F., and Madden, J. L.: Historical Aspects of Cardiac Resuscitation, Am. J. Surg. **70**:135-136 (Oct.) 1945.

18. Hosler, R. M.: Emergency Treatment of Cardiac Arrest, J. Internat. Coll. Surgeons **19**:336-340 (March) 1953.

ARTERIOGRAPHIC STUDIES OF THE CORONARY ARTERIES IN ISCHEMIC HEART DISEASE

Alan P. Thal, M.D., L. Stephen Richards, M.D., Richard Greenspan, M.D.
and
M. John Murray, M.D., Minneapolis

The coronary arteries have been visualized in unanesthetized patients by injecting a radiopaque medium through a catheter into the ascending aorta. After premedication with meperidine and atropine, the catheter is introduced by way of the brachial artery and inserted until its tip lies about 2.5 cm. above the aortic valve. Special techniques have been developed in order to predetermine the phase and duration of the injection, since 40 to 55 cc. of the radiopaque medium must be injected within 0.8 to 0.6 seconds and the subsequent film exposures must be properly timed. The most convincing sign of coronary artery disease is the roentgenographic finding of occlusion of a major vessel. Of the four illustrative case histories here given, two concern patients who had been considered for cardiac surgery because of signs and symptoms of angina pectoris; the arteriographic demonstration of normal coronary systems in both cases was decisive in planning subsequent treatment. Recently injections have been made during the first half of the cardiac cycle starting at systole. This has reduced the volume of contrast material needed by half without affecting the clarity of the arteriogram. In over fifty studies there have been no complications.

Recently developed techniques[1] permit the regular visualization of the blood supply of the heart in the unanesthetized patient. The fine detail of the studies now obtainable affords not only the means of precise localization of the occluding lesions of the major coronary vessels but also a detailed picture of the collateral vascular development. Apart from its investigative use, coronary arteriography is of value in elucidating difficult clinical problems and also in providing objective evidence of coronary disease prior to myocardial revascularization. The present paper serves to outline techniques recently developed in this institution. Representative cases will be illustrated.

Materials and Methods

Injection Apparatus.—In essence, the injection apparatus consists of a compressed nitrogen-driven syringe fired by a solenoid valve. The radiopaque medium in the syringe, being highly viscous, is warmed by a heat reflector. This injector is capable of delivering 65 cc. of a 90% solution of diatrizoate (Hypaque) sodium through a size 330 polyethylene catheter in one second. The detailed construction of the injector and delay circuit have been described in another paper.[1a]

Delay Circuit.—Our experimental and clinical studies have regularly shown that the best delineation of the coronary vessels is obtained by a rapid injection of concentrated dye timed to start at the beginning of systole and continue for one cardiac cycle. At heart rates from 60 to 80 beats per minute, the injection is carried out over a period of 0.8 to 0.6 seconds. To obtain precisely timed injections, a variable delay circuit has been utilized. The circuit is triggered by the R wave of the electrocardiogram and the duration of injection is varied according to the heart rate.

Catheterization of the Ascending Aorta.—While it is possible to gain access to the ascending aorta in various ways, it has seemed safest to us to adopt the route of the brachial artery. The artery is carefully exposed in the upper part of the arm, and a transverse arteriotomy is made. With use of a flexible catheter guide, the catheter is directed into the ascending aorta and positioned under the fluoroscope to lie about 1 in. above the aortic cusps. The guide is then withdrawn. After considerable trial, we have found a lateral-opening, closed-tip, size 330 polyethylene catheter to be most suitable for these studies. At the conclusion of the procedure, the catheter is withdrawn and a meticulous repair of the artery performed.

Preparation of the Patient.—Sedation is accomplished with meperidine (Demerol) hydrochloride, given intramuscularly prior to catheterization, and 0.6 mg. of atropine, given intravenously 10 minutes before the dye injection. The carotid arteries are manually compressed low in the neck during the injection to reduce the cerebral circulation of the opaque medium.

Radiopaque Mediums.—For detailed studies of the coronary circulation, it is necessary to use the newer concentrated mediums. Diatrizoate, in a 90% solution, has given satisfactory results in our hands. The viscous mediums require warming to body

From the departments of surgery, radiology, and medicine, University of Minnesota Medical School. Dr. Thal is an established investigator, American Heart Association. Dr. Richards is a research fellow, U. S. Public Health Service.

temperature prior to injection. The volume of material used has varied from 30 cc. to 50 cc., depending on the size of the patient and the heart rate.

Calibration.—With use of a two-channel recording unit, a simultaneous electrocardiographic and aortic pressure curve tracing is made. The delay between the peak of the R wave and the peak of systole is measured and the delay circuit calibrated accordingly. A trial run is then made with the injector excluded from the circuit. The precise phase and duration of injection is then recorded. In general, at a pulse rate of 70 to 80 per minute, the actual injection can be made over 0.8-0.6 seconds. This allows for the injection of 40 to 55 cc. of radiopaque material.

Rapid Film Changer.—The Schonander biplane unit, which allows six films per second in two planes, has proved satisfactory for detailed studies of the coronary circulation. As has been shown in peripheral arteriography, films taken in one plane may give an erroneous idea of vessel caliber. The anterior descending branch of the left coronary

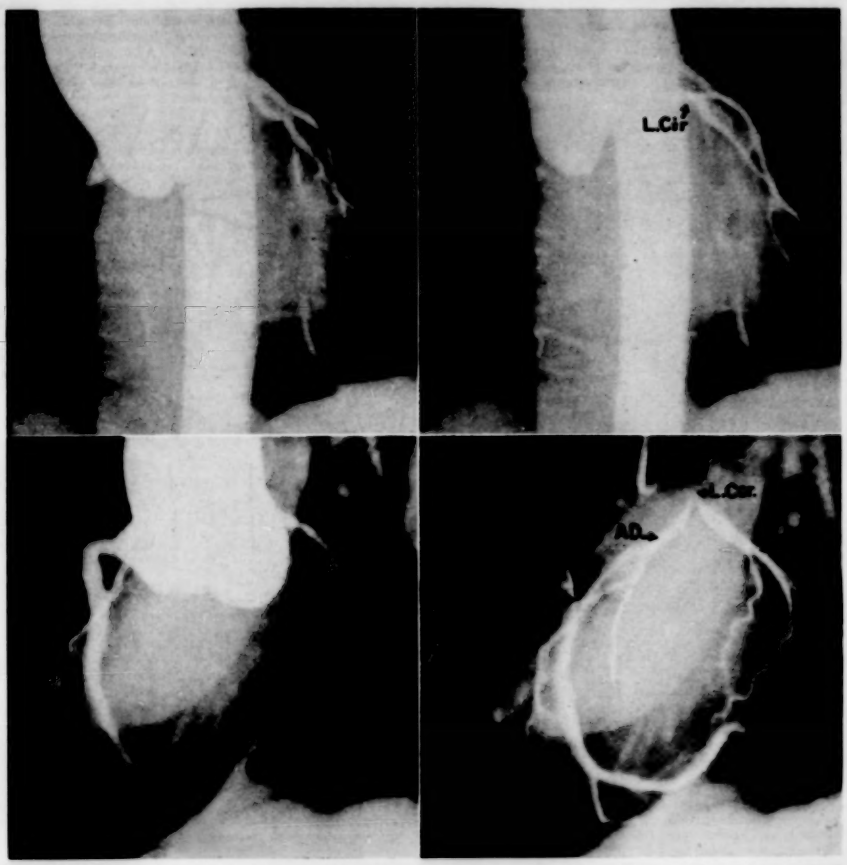


Fig. 1 (case 1).—Anteroposterior and lateral views of corona y arteriogram in patient with angina-like symptoms. Arteriogram shows entirely normal pattern. *L. Cor.* indicates left coronary artery; *R. Cor.*, right coronary; *L. Cir.*, left circumflex branch; *AD*, anterior descending branch; and *PD*, posterior descending coronary artery.

artery is best seen in the posteroanterior view, while the right coronary and left circumflex branch are best studied in lateral view.

The following cases were selected to demonstrate the value of coronary arteriography both in the resolution of difficult clinical problems and in the investigation of the pathological anatomy in severe coronary sclerosis.

Report of Cases

CASE 1.—A 55-year-old woman was first seen on March 18, 1958, with a three-year history of chest pain on exertion. The pain was described as being retrosternal with radiation down the left arm to the wrist. It would occur initially only on moderately severe exertion and, at that time, was promptly relieved by cessation of activity. The severity and frequency of the pain increased, requiring nitroglycerin for relief. When first seen, pain would occur spontaneously at rest and she had been taking meperidine, promazine (Sparine) hydrochloride, and occasional injections of morphine sulfate for relief. She was described as being extremely dependent on her doctors. She was apparently subject to moderately severe depression. This patient was referred to the University Hospitals for surgical revascularization of the heart. The physical examination revealed a mild degree of rheumatoid arthritis involving the proximal interphalangeal joints of the hands only, a blood pressure of 120/90 mm. Hg, a pulse rate of 84 per minute which was regular, no evidence of displacement of the apex beat, no abnormal heart sounds or murmurs, and no evidence of congestive heart failure. An electrocardiogram taken when she was at rest revealed no abnormalities. In view of the patient's personality problem and her knowledge of the symptoms of coronary artery disease, it was felt that there was considerable doubt about the diagnosis of angina pectoris. Accordingly, a coronary arteriogram was performed. This is illustrated in figure 1 and is interpreted as showing a normal coronary system. When the patient was confronted with this evidence, the chest pain disappeared. However, within a few days she developed pain in her legs, of similar character.

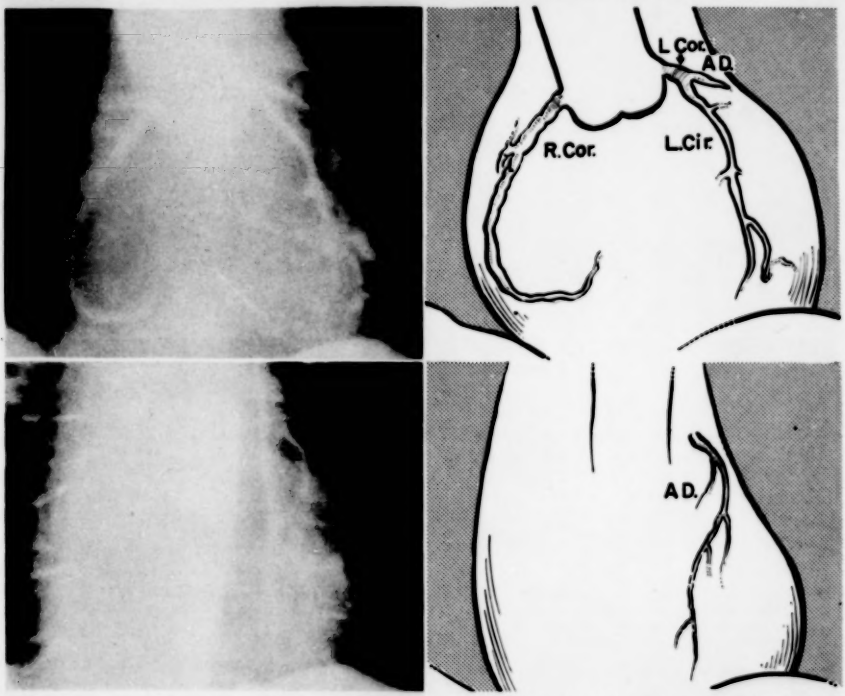


Fig. 2 (case 2).—Arteriograms with corresponding drawings (*top*), showing generalized narrowing and irregularity of whole coronary system with complete occlusion of anterior descending coronary artery near its origin and (*bottom*), taken several seconds later, demonstrating reflux filling of anterior descending coronary artery from collaterals over apex of heart.

CASE 2.—A 53-year-old man was first seen on March 11, 1958, complaining of chest pain on exertion, which had been present for 18 months but had become worse since July, 1957. He first noticed the onset of retrosternal squeezing pain with radiation to both arms while working or walking. Initially, the pain was relieved promptly by ceas-

ing activity or by taking nitroglycerin. The condition progressed so that at the time of admission even the mildest exertion precipitated pain lasting up to 10 or more minutes. The physical examination was entirely unrevealing, the blood pressure being recorded at 140/85 mm. Hg, with no evidence of cardiac enlargement, abnormal heart sounds, or murmurs. There was no enlargement of the heart on x-ray, but the electrocardiogram showed inversion of T waves in leads 1, aVL, V_5, V_6, and V_5 consistent with myocardial ischemia. Coronary arteriograms (fig. 2) demonstrated complete occlusion of the anterior descending branch of the left coronary artery, with diffuse atherosclerosis of the whole coronary system. It is of interest that intercoronary collateral flow was well established and there was retrograde filling of the occluded anterior descending artery. This patient obtained some immediate subjective improvement after pericardial poudrage.

Case 3.—A 52-year-old man was first seen on Dec. 20, 1957, complaining of chest pain on exertion since 1955. Initially, the pain occurred on exertion or in the early hours of the morning, when it awakened him from sleep. It was retrosternal, with radiation into the left arm to the fingertips. Initially, it was relieved by nitroglycerin, the efficacy of which became less as time went on. On May 27, 1957, he had an attack of severe chest pain at which time a diagnosis of myocardial infarction was made. After this he continued to have attacks of pain at rest and on mild exertion, as well as during the night. Physical examination revealed a blood pressure of 150/90 mm. Hg, no cardiac enlargement, and no congestive heart failure, but the presence of an atrial gallop in the apical region was noted. The electrocardiogram taken at rest was reported within normal limits, and the chest x-ray confirmed the absence of cardiac enlargement. The serum cholesterol level was recorded as 272 mg.%. Coronary arteriograms revealed generalized narrowing of the whole coronary system with multiple and extensive occlusions of the anterior descending branch of the left coronary artery. There was prominent filling of small extracardiac vessels at the base of the heart in the anterior mediastinum. These presumably represented expansion of the vessels over the pulmonary conus. Subsequently, the internal mammary artery was implanted into the myocardium. The patient tolerated this well. However, about two hours after operation he died suddenly in ventricular fibrillation. The extreme degree of atherosclerosis is illustrated in figures 3 and 4. The possibility exists that disruption of anterior mediastinal collateral vessels during mobilization of the internal mammary artery further diminished an already marginal blood flow to the heart.

Case 4.—A 24-year-old woman was first seen on Jan. 13, 1958. Heart trouble was apparently initially suspected at the age of 9 years, when a cardiac murmur was first noted and attributed to rheumatic fever. She remained reasonably well, however, apart from easy fatigability on strenuous exertion, until 1955, at which time she noticed shortness of breath spontaneously and on exertion. For one year she had noticed fleeting stabbing pains located in the center of the anterior part of the chest; this seemed to be worse after exertion. Two weeks before admission she had noticed a severe generalized crushing pain in the anterior part of the chest, lasting two minutes and associated with shortness of breath and sweating but apparently unrelated to exertion. Examination revealed no cardiac enlargement, a blood pressure of 100/70 mm. Hg, and a pulse rate which was regular at 68 per minute. There was no evidence of congestive heart failure, but there was a loud third heart sound audible both at the apex and along the left sternal border, while at the pulmonic area there was a moderately loud systolic murmur of the ejection type.

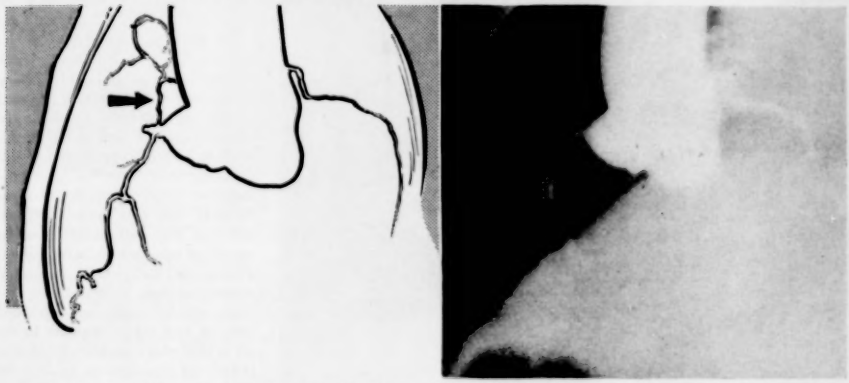


Fig. 3 (case 3).—Extreme coronary sclerosis with occlusion and recanalization of left main coronary. Lateral view shows extensive collateral vessels anterior to aorta. This trunk represents ramus ostii cavae superioris, which takes origin from right coronary artery.

The pulmonary second sound was not accentuated and was normally split. The electrocardiogram revealed inversion of T waves in leads 2, 3, aVF, V_2, V_3, V_4, V_5, and V_6, as well as depression of the ST segments in leads 2, 3, aVF, and V_6. This electrocardiogram showed no change over one taken four years previously. Cardiac fluoroscopy revealed a heart well within the normal limits of size and configuration, although there was a question of right ventricular enlargement. Right heart catheterization was performed, and the findings were entirely within normal limits. It was felt that possibly this woman had an anomalous origin of one coronary artery to account for what resembled either ischemic heart disease or a myocardiopathy of unknown origin. A coronary arteriogram was taken. As shown in figure 5, this showed a completely normal coronary system.

Arteriographic Signs of Coronary Artery Disease

The most definitive sign of coronary arteriosclerosis seen on angiography is a complete or partial occlusion of a major vessel. This is most commonly seen in the proximal reaches of the anterior descending branch of the left coronary artery and may be manifested by a gradual tapering of the vessel lumen, by a complete and abrupt obstruction to the column of dye, or by an atheromatous encroachment on the lumen. Frequently, small tortuous vessels can be seen bypassing such an occlusion or feeding its distal portion by collateral from an adjacent artery. While these occlusions may form the most striking feature of a coronary arteriogram, diffuse disease of the whole system is shown by gross irregularity of the intimal surface and rigidity of the vessel during systole and diastole. In aged patients without evidence of myocardial ischemia, extreme tortuosity and microaneurysm formation is common. A complete and dynamic impression of the coronary topography in disease can only be secured by viewing multiple films taken in two planes. In this way, retrograde filling of an obstructed coronary artery may be seen in late films.

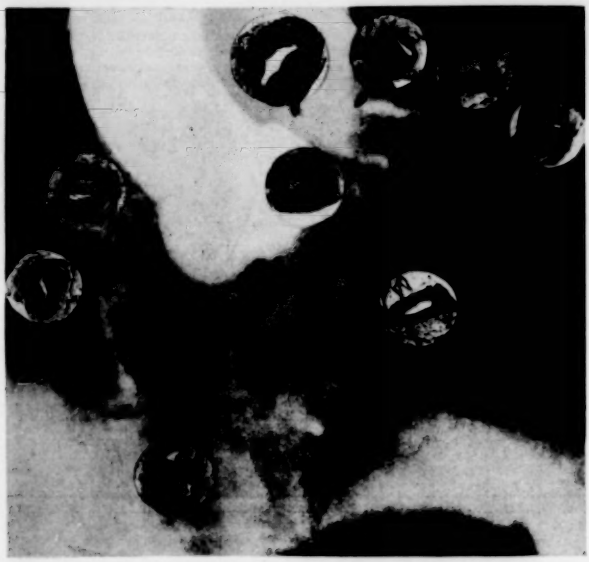


Fig. 4 (case 3).—Sections of coronary arteries shown superimposed on arteriogram of patient with severe angina at rest. Extreme degree of narrowing extending far out into periphery is shown.

Another sign which is encountered only in patients with extremely advanced disease is stasis of radiopaque material in peripheral areas of the coronary circulation, where proximal obstruction has brought about considerable slowing of the blood flow. In two patients with intractable angina pectoris at rest, we have demonstrated extensive atrial and anterior mediastinal collateral vessels. These vessels appear to be expansions of the normal small vessels at the base of the heart emanating from both right and left coronary arteries and normally ramifying over the atria, the pulmonary conus, and the superior vena cava. It is quite possible that they represent an expanding collateral circulation which develops as a result of extreme ischemia. The branching vessels seen anterior to the aorta in figure 3 represent the ramus ostii cavae superioris [2] which supplies the sinoatrial node and forms collaterals around the atria, with the pericardiophrenic artery, and other extracardiac vessels.

Comment

In 1955 we developed techniques for direct anastomotic bypass of experimental coronary occlusion.[3] This work was based on the premise that the coronary arterial disease was often localized to the first portions of the main coronary arteries. Our subsequent arteriographic studies suggest that this concept is erroneous. The patient with angina on effort appears to have diffuse disease of the whole coronary arterial system, while in the patients we have studied with angina at rest there appears to be an additional impairment of the collateral circulation. In the 50 patients we have now studied there have been two instances of segmental arterial block. Both of these patients are asymptomatic. This situation is quite analogous to that seen in the experimental animal, which survives a punctate occlusion in the presence of an otherwise normal coronary vasculature. These findings then make it appear unlikely that direct coronary artery surgery will be effective in the treatment of ischemic heart disease.

While the diagnosis of myocardial ischemia can frequently be made with great accuracy on the basis of the history and electrocardiographic findings, yet there remains a small but definite group of patients in whom the diagnosis remains in doubt in spite of careful clinical study. These problem cases may readily be resolved by coronary arteriography, which, in our experience, may now be done with small risk and little discomfort to the patient.

It is now apparent from the results of various types of surgical procedures for myocardial revascularization that there is a strong functional element in many patients with angina pectoris. The extent of this functional overlay can be judged from the occasional patient with established angina pectoris who obtains complete relief of his symptoms after nothing more than a skin incision. Within the last eight months, among the patients referred to this hospital for myocardial revascularization operations, four were found to have entirely normal coronary arteriograms and in each instance the chest pain was greatly ameliorated or disappeared after the patient was informed that the coronary system was normal. The percentage of such patients included among the successful results of myocardial revascularization is unknown, but it is apparent that coronary arteriography would be of value in eliminating this type of patient as a surgical candidate.

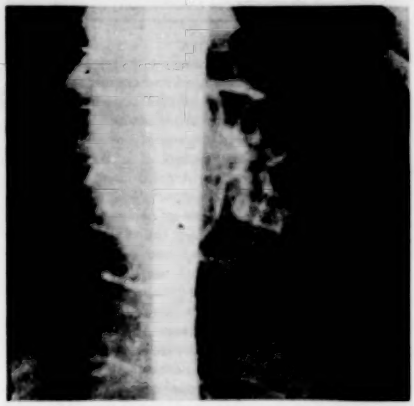


Fig. 5 (case 4).—Coronary arteriogram, showing entirely normal pattern. Large, smooth-walled vessels may be contrasted with extreme narrowing seen in figure 3.

Quite apart from the diagnostic value of these studies, it may be possible with increased experience to formulate a more accurate prognosis in coronary sclerosis based on such factors as the extent of the disease and the collateral response. Last, but perhaps most important, the method offers a basic research technique for evaluation of the early vascular reactions to ischemic myocardial insult.

Summary

Recently developed techniques for coronary arteriography have made possible a quality of arteriogram which allows critical study of the coronary arterial system in patients with severe coronary sclerosis. In four representative cases, two patients originally referred for surgical treatment were shown to have normal coronary vessels. The most definitive roentgenologic sign of coronary artery disease is complete or partial occlusion of a major vessel.

This study was supported by grants from the U. S. Public Health Service and the Minnesota Division, American Heart Association.

The diatrizoate sodium used in this study was supplied as Hypaque-M, 90%, by Winthrop Laboratories, New York.

References

1. (*a*) Richards, L. S., and Thal, A. P.: Phasic Dye Injection Control System for Coronary Arteriography in Human, Surg. Gynec. & Obst. to be published. (*b*) Thal, A. P.; Lester, R.; Richards, L. S.; and Murray, J.: Coronary Arteriography in Arteriosclerotic Disease of the Heart, Surg. Gynec. & Obst. **103**:457-464 (Oct.) 1957.

2. James, T. N., and Burch, G. E.: Atrial Coronary Arteries in Man, Circulation **17**:90-98 (Jan.) 1958.

3. Thal, A.; Perry, J. F.; Miller, F. A.; and Wangensteen, O. H.: Direct Suture Anastomosis of Coronary Arteries in Dog, Surgery **40**:1023-1029 (Dec.) 1956.

PROGNOSIS OF MYOCARDIAL INFARCTION.—As emphasized in the 1941 and 1956 reports, the most important clue favoring longevity and a return to a normal program of life [in 200 patients with coronary thrombosis and myocardial infarction] was found to be the degree of completeness of recovery after the first month of convalescence from the acute attack. Of the 24 cases who showed neither myocardial nor coronary insufficiency, 18 (75%) survived five years, while the average survival of these 24 cases was 12 years. Among those who, free of complications, completely recovered from their attack, the eventual cause of death was most commonly coronary, either recurrent thrombosis or sudden death, with or without evident angina pectoris. . . . Not infrequently during the 1920's the treatment and cooperation of patients . . . were inadequate. . . . Our attitude concerning the prognosis of coronary thrombosis with myocardial infarction will undoubtedly be much more optimistic in the future than it has been in the past because of the recognition of mild cases, the better treatment and program after recovery, and the more satisfactory understanding and cooperation of the patient.—P. D. White, M.D., E. F. Bland, M.D., and S. A. Levine, M.D., Further Observations Concerning the Prognosis of Myocardial Infarction due to Coronary Thrombosis, *Annals of Internal Medicine*, January, 1958.

SOME NEW CONCEPTS OF CORONARY HEART DISEASE

RESULTS AFTER SURGICAL OPERATION

Claude S. Beck, M.D., David S. Leighninger, M.D., Bernard L. Brofman, M.D.
and
Jess F. Bond, M.D., Cleveland

In disease of the coronary arteries the myocardium is handicapped and endangered by ischemia; correction of this condition is the aim of the operation described here. With the patient under general anesthesia, the pericardium is opened. The parietal pericardium is abraded. A constricting ligature is usually placed about the coronary sinus, and before the end of the operation it is tightened to narrow the sinus to a diameter of 3 mm. Powdered asbestos is lightly sprinkled over the surface of the heart. The parietal pericardium is not closed, but the pericardial fat is sutured over the exposed surface of the heart. The mortality rate from this operation was found to depend entirely on how high a percentage of patients with advanced coronary disease were included in the series. In 110 patients with initially poor prognosis approaching the terminal stage, the hospital mortality was 11%; among the remaining 234 patients, the hospital mortality was 3%. Subjective benefits from the operation included relief from pain and reduced intake of medicaments. Objective evidence of benefit included return to gainful occupation, rise in skin temperature of extremities, disappearance of arrhythmias, and increased force of heartbeat as recorded by ballistocardiogram. The lasting effects of the operation contrasted strongly with the temporary effects of medication.

Direct operative procedures carried out on the heart and on the coronary blood vessels of dogs have yielded some new and different points of view concerning coronary heart disease.[1] Reference is made to it as a background for this report, which concerns the operation on humans.

Effective Treatment

The starting point for effective treatment of coronary heart disease concerns blood supply to ischemic muscle. Any medicament or any surgical operation that increases the amount of blood in ischemic muscle (distal to stenosis or occlusion in an artery) is obviously beneficial. This statement may be considered as an axiom or as a self-evident truth concerning treatment of this disease. Addition to this amount of blood is beneficial; reduction has the opposite effect.

Total Coronary Artery Inflow.—The myocardium requires a certain amount of blood to sustain the heart beat. The total capillary flow for the human is about 250 cc. per minute and for the dog about 100 cc.[2] The normal coronary arteries are capable of carrying much larger quantities than these amounts, and, therefore, the arteries can be narrowed severely before inflow becomes inadequate. Inadequate inflow is one of the factors that kills, and it occurs with or without infarct in the muscle.

Several surgical operations have been devised to increase total inflow. In general, the statement can be made that the heart resists the entrance of outside blood. It is not impossible to add blood to the heart because specimens exist which demonstrate blood vessels between grafts placed on the heart and the heart itself, and these are large enough to carry blood, but they cannot be produced with any degree of regularity. Perhaps better grafting methods can be developed in the future. Another approach to augment inflow consisted of putting arterial blood into the coronary sinus and diverting it in a retrograde direction through the capillary bed. This works satisfactorily for about six weeks, and then intimal thickening in the veins begins to block off inflow. However, the heart is protected by another mechanism (to be discussed later) after retrograde flow no longer occurs. Another possibility for the addition of blood concerns surgical procedures on the diseased arteries themselves.

Restoration of Lumina of Coronary Arteries: To clean out the debris from these arteries (endarterectomy) and to reestablish their lumina is an attractive idea because, being an extirpation procedure, it is readily understood. The question is: "Can it be done successfully in arteries of such small size and also when the disease is usually widespread and rarely localized to one short segment of artery?" Experience with this procedure is being

From the Western Reserve University School of Medicine, the University Hospitals, and Mount Sinai Hospital.

Read before the Section on Surgery, General and Abdominal, at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

obtained, and this should give an answer to this query. Our experiences on the dead heart indicated that endarterectomy will probably not be successful. The disease usually extends into secondary arterial branches, and manipulation of a stenosed artery may produce occlusion of the artery.

Distribution of Blood in Coronary System: The heart enjoys an even distribution of the blood that gets through the diseased arteries. In many patients with the disease there is enough blood getting into the heart to provide adequate function, but its distribution is at fault. It is an uneven or checkerboard distribution, and this produces pain and self-electrocution of the heart. Indeed, this is the most common cause of death. It occurs when the patient is on the golf course, while he is shoveling snow, watching athletic contests, in the office, at work, and so on and often in hearts that anatomically are too good to die. It is a physiological type of death, and the coroner or pathologist is often hard pressed to explain it. There may be no infarct and no occlusion, only narrowing of an artery. In the experimental laboratory and by successive operations all coronary arteries in the dog were occluded except for a 1-mm. lumen in the circumflex artery, and these dogs were active and in good health.[3] The factor that made these occlusions possible was the presence of a good set of intercoronary vessels that were produced by surgical operation before the arteries were occluded, so that a red blood cell,

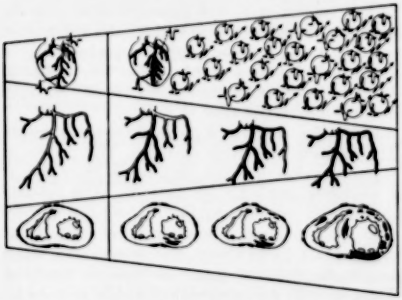


Fig. 1.—Death factors in coronary heart disease. *Top*, uneven distribution of blood producing oxygen differentials and electric condition that can destroy heart beat. *Center*, reduction of inflow; not enough blood to support heart beat. *Bottom*, muscle destruction; not enough muscle to maintain adequate circulation; death results from myocardial failure.

once it got past the stenosis in the circumflex artery, could go anywhere within the substance of the heart where it was needed most. Enough blood to support the heart beat can go through an opening of 1 mm. in diameter. In the human enough blood to support the heart beat can go through a stenosis of 1.5 mm. in diameter. A good set of intercoronaries is necessary to prevent fibrillating currents as stenosis and occlusion progress to the terminal stage of inflow reduction.

Muscle Failure.—Another way by which the disease kills is by destruction of muscle. One artery after another becomes occluded; one segment of

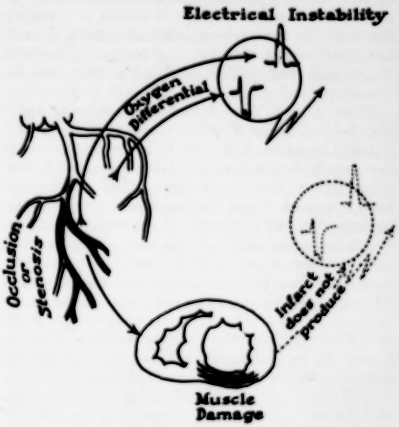


Fig. 2.—Two sequelae which may occur after stenosis or occlusion of artery. One is unstable electric condition due to oxygen differentials in muscle and other is infarct.

muscle after another becomes scarified; there is not enough muscle to produce effective blood pressure; the patient dies in failure. The heart escaped fibrillation while these occlusions occurred. The electric alterations produced by occlusion were never strong enough to kill, and, indeed, the total inflow might be adequate to support the heart beat. This has been referred to as muscle death. The three death factors in the disease are shown in figure 1.

Two sequelae of occlusion are shown in figure 2. Occlusion produces an oxygen-differential in contiguous areas of muscle which in turn produces anginal pain and an electric condition that can fibrillate the heart. Also, occlusion may produce death of muscle. These two sequelae are not related. The heart can electrocute itself in the absence of an infarct. Likewise an infarct can develop without electrocuting currents. It is well to bear these facts in mind because the diagnosis of a mild occlusion is often made and the patient dies. A human can have a small infarct but not a mild occlusion. A mechanism that has the potential of death should scarcely be referred to as "mild."

Value of Operation.—There are certain things that surgical operation can do and there are certain things that it cannot do. Let us consider the three death factors of the disease. For oxygen differen-

tials, anginal pain, and electric instability surgical operation is beneficial, and it is beneficial because it produces intercoronary vessels. For inflow reduction which is approaching the terminal stage surgical operation is probably not effective; perhaps more effective methods can be developed. For muscle damage operation is not effective; muscle cannot be restored. Self-electrocution is always a threat in the presence of coronary artery disease. Intercoronaries are always a protection against this factor, and they protect until inflow reduction becomes terminal.

Blood Supply into Ischemic Muscle, as Influenced by Glyceryl Trinitrate and by Operation.—A large number of backflow determinations have been made in our research laboratory, and a considerable experience with this method of study has been acquired. These measurements are important because they are a measure of the amount of blood that is in a segment of ischemic muscle. This method measures the axiom of treatment. These measurements are done by ligating the circumflex artery at its origin and then cutting the artery distal to the ligature. A cannula with two connections is inserted into the cut artery so that backflow from the artery can be collected and measured and also for perfusion of the artery between determinations by a connection with the carotid artery. Measurements of backflow are made for 30 seconds; then the artery is perfused from the carotid in order to preserve the heart beat.

The effect of glyceryl trinitrate was measured by 43 determinations on 21 normal dogs. This drug increased backflow an average of 0.88 cc. or 10 drops per minute. The range was from 0.0 to 4.0 cc. Statistically these figures are highly significant. The drug-effect lasts for about five minutes. The statement can be made that this drug adds blood to ischemic muscle from adjacent muscle with a good blood supply. This addition of blood reduces the differences in oxygen content in muscle and helps to bring about a more even distribution. This in turn reduces pain and, no doubt, protects the heart. The drug-action is temporary. This drug does not produce intercoronary vessels. The Beck operation adds 4.7 cc. or 47 drops per minute to the quantity already there, and it is a permanent addition. Patients having used this drug while on a medical regimen and then later having gone through surgical operation are in a position to evaluate and compare both forms of treatment. The clinical benefit obtained by these patients from this drug and from surgical operation gives new significance to 10 drops and 47 drops, respectively, per minute to ischemic muscle as produced by these two forms of therapy.

Preoperative Considerations

The ideal patient for operation is one who has anginal pain and an adequate total arterial inflow. The patient with adequate inflow needs a more even distribution and operation accomplishes this. It need scarcely be stated that anatomic disease in muscle and/or arteries cannot be eradicated by surgical operation. A patient with severe muscle destruction and failure is not acceptable for operation nor is the patient with terminal disease in the arteries. Inflow reduction approaching the terminal stage may occur in hearts that do not have a gross infarct. These hearts are irritable at operation, and they are susceptible to fibrillation. This condition cannot always be recognized before operation.

The studies carried out before operation are not more extensive than necessary. They consist of fluoroscopic and x-ray examination of chest, electrocardiogram with or without exercise, the ordinary laboratory tests, and special studies only when indicated. Diagnosis is often based on a good history. If there is any doubt concerning diagnosis, operation is delayed or not done. Operation is delayed if there is any recent activity in the disease. It is not done within six months after an infarct. A serious program against obesity is carried out before operation. Almost all of our patients stop smoking and do not take it up later. The mental attitude of the new patient is helped by talking to patients who have been operated on. The patients operated on are very willing to do this. The patient is told that if his blood pressure falls while he is under anesthesia, operation will not be done. This reduces the disappointment if it is not done. He is told to expect incisional pain and that pills for anginal pain will be at his bedside. He is told that when he awakens in the recovery room he will have a tube in his nose for oxygen, that a tube will be in his chest for drainage, and that a needle will be in a vein for administration of fluid.

Instruction concerning physical therapy is given. This consists of several exercises. The patient is taught postural drainage lying on the right side at a 45-degree angle for 15 minutes. After postural drainage the patient coughs for about five minutes while an attendant splints the lower part of the chest with a towel drawn taut around him. He is taught diaphragmatic and abdominal breathing. These muscles are used while the chest is in an expanded position. Arm and shoulder exercises are done. The range of motion is determined before operation, and this amount of motion is obtained after operation. Postural drainage, coughing, diaphragmatic breathing, and arm-shoulder exercises are taught before operation and are resumed the day after operation and done three times daily for one week. They reduce pulmonary complications and prevent the development of a frozen shoulder. They also reduce the reaction of being an invalid after operation, and the patients do not object to them after they once get started.

Technique of Operation

The patient is given a general anesthetic. An intratracheal tube and a mechanical respirator are used. The patient is connected to a cardioscope.

Fig. 3.—Latissimus dorsi muscle is elevated. Intercostal muscles are cut between fifth and sixth ribs for length of about 25 cm. Inset shows position of patient on operating table and location of skin incision.

Relaxing drugs and light anesthesia are used. The patient is turned on his right side. If the arterial pressure should fall below 90 mm. Hg and if it does not recover within 30 minutes without the use of pressor drugs, use of the anesthetic is discontinued and operation is not done. A fall in pressure indicates severe inflow reduction. The incision is placed between the fifth and sixth costal cartilages and ribs and is about 20 cm. in length. The latissimus dorsi muscle is elevated, and the intercostal muscles are undercut (fig. 3). A self-retaining retractor is placed, and the ribs are spread apart about 10 cm. (fig. 4).

The blood supply to the fat on the pericardium is preserved as much as possible. The pericardium is opened from apex to base, and traction sutures are placed in the pericardium (fig. 5). The heart is examined and data are obtained as follows: the size of the heart—normal or enlarged; character of beat—uniform, a roll (indicating a scar), or reduced or absent pulsation in any area; a bulge or aneurysm; irritability to touching; soft, thickened, or calcified common left artery as indicated by light palpation with a finger; streaking, beading, or reduced pulsation in descending artery and its branches and the branches from the circumflex artery; and infarct on the surface. The heart is tipped up for examination of the posterior surface (fig. 6). Occasionally this cannot be done because of irritability.

If the common left artery is soft one can conclude that inflow is satisfactory, that distribution is the problem, and that a favorable result can be expected. If the anatomic disease is not severe, a good prognosis can be given; if it is severe, it is classified as salvage and a guarded prognosis is given. The lining of the parietal pericardium is abraded; care is taken not to stretch or contuse the left phrenic nerve. The heart is gently rotated to expose the coronary sinus. A needle carrying a piece of silk is passed around the sinus about 2 cm. from the point where it empties into the right auricle. Usually the middle cardiac vein empties into the sinus beyond this constricting ligature. If the heart is enlarged so that exposure of the sinus is difficult

Fig. 4.—Special retractor on lung. Left phrenic nerve and fat on outside of pericardium are shown.

or if the heart is irritable or if the sinus is covered with fat and cannot be located, this part of the operation is omitted.

The next step consists of gentle abrasion of epicardium between branches of the arteries and making a light application of 5% aqueous solution of trichloroacetic acid freshly prepared to the surface

of the heart between the secondary branches of the major coronary arteries. If the heart is irritable, abrasion is omitted. The next step consists in narrowing the coronary sinus to a diameter of 3 mm. This is done by tying a knot in the silk already

Fig. 5.—Pericardium opened medial to phrenic nerve; traction sutures in pericardium; heart exposed. Branches of descending and circumflex arteries are seen. Infarct is in left ventricle. Branches from descending ramus showed reduced pulsation.

placed over a probe of this size and then removing the probe. A light sprinkling of powdered asbestos is placed on the surface of the heart. The parietal pericardium is not sutured, but the fat is sutured so as to cover the anterior aspect as much as possible as a graft. This complete procedure is carried out when the heart is stable and tolerates manipulation. If the heart is irritable, the operation is limited to application of trichloroacetic acid and powdered asbestos. A tube with an underwater seal or suction is placed low in the midaxillary line for 48 hours. The intercostal nerves on the left are injected with tetracaine (Pontocaine) hydrochloride before closure is done. Oxygen is given through an intranasal tube for several hours.

It is possible to do the operation with a low mortality. We did 100 consecutive operations with zero mortality. If patients with severe inflow disease are selected, then there will be some mortality. Such patients would have a limited expectancy without operation. When operating on hearts that are very irritable, the extent of the procedure is reduced. Some of these hearts can scarcely be touched at operation. In such cases the application of trichloroacetic acid and asbestos powder constitute the operation.

Use of Drugs.—All patients are digitalized before operation. The drugs used preoperatively are morphine, pentobarbital sodium, and atropine. In the operating room the patient is given glyceryl trinitrate if he has anginal pain and promethazine (Phenergan) hydrochloride, 0.0373 to 0.050 Gm., is given intravenously if the patient is apprehensive. The patient is well ventilated with oxygen. Thiopental (Pentothal) sodium and succinylcholine chloride are given intravenously. An intratracheal tube is inserted. Respiration is usually assisted because of apnea and on resumption of spontaneous respiration *d*-tubocurarine chloride is given and respiration is taken over by the Rand-Wolfe respirator. The use of a mechanical respirator is recommended. Anesthesia is maintained with nitrous oxide and a small amount of ether. Tubocurarine is given as necessary to control the motion of the diaphragm. Plane 1 anesthesia is used throughout the operation, and analgesia is used for closure. The patient is awake when the intratracheal tube is removed.

Fig. 6.—Apex elevated showing posterior aspect of heart.

If the pressure falls or if the heart rate is rapid or irregular, use of anesthetic is discontinued, and the lungs are well ventilated for several minutes. Mephentermine (Wyamine) in a dosage of 15 mg. is given intravenously for its pressor effect. Procainamide (Pronestyl) hydrochloride, in dosage of 50 to 100 mg., is given intravenously to reduce the

irritability of the heart. A slow heart rate is preferable to a rapid rate, and atropine should be used only with caution. If the rate is 120 per minute or more, lanatoside C (Cedilanid), in a dosage of 0.2 to 0.4 mg., is given intravenously. It takes effect in about 20 minutes; often the rate falls abruptly to 80 per minute. During this waiting period the lungs are well ventilated. Quinidine sulfate, dosage 0.4 Gm. intravenously, is rarely used for frequent extrasystoles. The most effective way to take care of these is to reduce manipulation of the heart or to give it complete periods of rest or not to handle it at all.

Postoperative Care

The patient is conscious when the dressing is applied to the wound and when the intratracheal tube is removed. The patient is placed in semi-Fowler's position, given oxygen nasally, and kept in the recovery room for about five hours. Glucose solution is given intravenously, but the needle is removed after several hours. After return to his room, the patient sits up and dangles his legs or sits in a bedside chair. Sedation is kept to a minimum. Coughing and arm movements are encouraged. On the next day the patient stands on his feet for about 30 minutes, three times. The physiotherapist takes over for exercises the first day after operation and continues for one week. On the second day the tube is removed from the chest. Use of antibiotics and digitoxin is discontinued after one week. One, sometimes two, x-rays of the chest are taken after operation. Discharge from the hospital occurs on the 10th to the 14th day after operation.

The complications are few. In one patient the heart began to fibrillate and stopped beating four hours after operation. This occurred in the recovery room, which is near the operating room. One of us (C. S. B.) was operating on another patient when it occurred. He immediately left the operation, opened the chest while the patient was in the recovery room, pumped the heart for 35 minutes, and shocked the heart out of fibrillation; the patient is alive with no mental deficit and little or no anginal pain two years later. In several other patients fibrillation occurred, but the heart beat could not be restored. In these we tried unsuccessfully to clean out a coronary artery. Other complications were an embolus to an arm, and this embolus was successfully removed; mesenteric thrombosis occurred, and the artery was cleaned out, but it clotted again and the patient died. Complications have been few.

Early Observations After Operation.—The sedative effects of the surgical procedure are passed off by the second or third day. At this time when the patient is asked how he feels, he usually states that his chest hurts and points to the incision. When asked how his heart feels he usually states "It feels alright; I have not noticed that I have a heart; it feels free and looser; it isn't tight." How about pain? "I have not had any of the old heart pain; my arm feels better, and I feel warmer." This type of early report occurs in the majority of patients. Before discharge from the hospital the patient is allowed to try himself out on two or three flights of stairs. To the patient and to us doing this work, the reaction of the patient to exercise is most gratifying.

On discharge from the hospital the patient is told not to expect too much because his disease has not been cured, that after increased physical exertion he may have some pain, that he should not hesitate to take a glyceryl trinitrate pill for it, and that his improvement will continue over a period of several months.

Mortality.—Mortality depends to some extent on the type of patient selected for operation. If operation were applied only to patients in the terminal stages of this disease the mortality would be prohibitive. On the other hand, if it were applied only to patients with slight disease, the mortality would be zero or almost zero. Our policy is not to aim at zero mortality, because in achieving such a record patients who need help and who could be rehabilitated to a work-status would be denied operation. One-third of our patients have advanced disease as determined by examination of arteries and muscle at the time of operation. These patients are classified as salvage.

From Jan. 1, 1954, to Feb. 14, 1958, the Beck operation was done on 347 patients. These were consecutive operations done at University Hospitals and at Mount Sinai Hospital, Cleveland. During the period of hospitalization the total mortality was 21, or 6%. The total mortality after discharge from the hospital during a period of somewhat more than four years was 32, or 9.2%. Within this series were 100 consecutive operations with zero operative mortality, and in the subsequent series of 100 cases there were four patients who died, making the mortality 2% in 200 consecutive cases.

In the 110 salvage cases the hospital mortality was 11%, and the subsequent mortality was 15% for a total of 26%. In the 234 nonsalvage cases the hospital mortality was 3%, and the subsequent mortality during the four-year period was 7% for a total of 10%. There were three patients not classified. In the nonsalvage cases, the risk of operation is small and the life span appears to be excellent. In patients with coronary heart disease this record emphasizes the desirability of early operation. The death factor in the early stages of the disease is electric imbalance, and operation is especially designed for this factor.

Clinical Results

Relief of Pain.—Relief of pain is experienced within a few days after operation. Even at operation the heart is less irritable toward the end of the procedure than when it was first touched. A scratch on the skin to mark the incision becomes a band

of red within a few moments. Similar changes are, no doubt, possible in the heart, and the heart is extremely responsive to any changes in blood supply.

A survey of clinical results was completed recently. In this series of 347 patients, 295 patients are now living. Each of these was contacted. Two hundred seventy-eight of these patients, 94%, received an excellent result (32%) or a good result (62%). The definition of an excellent result is applied to those who are completely or almost completely free of pain and have taken no medicaments since operation. The definition of a good result is applied to those patients who are improved after operation but who have an occasional pain and who take significantly less medicaments than before operation. The results in the 73 living patients classified as salvage are almost as good as those obtained in the other group. The percentage of excellent results, 22%, is less, but the percentage who received improvement was as high or even higher than in the other group. Because of this we believe the restrictions for acceptance of patients for operation should be as broad as possible, even though it involves increased mortality.

The patients herein analyzed have had the experiences of medical treatment first and surgical operation later. These patients, therefore, can compare the relative merits of medical and surgical therapy. The superiority of surgical versus medical treatment is in about the same proportion as measured in the laboratory or about five to one in favor of surgical operation. Furthermore, the surgical result is permanent while the drug-effect is transient. Many of the patients were disappointed with medical therapy and were critical of their professional care, in that operation had been delayed or that the patient had even been advised not to have the operation done. This reaction by the patients was intensified by the knowledge that medicaments fail to produce intercoronaries and that all they were receiving from the medication was transient relief of pain. To these patients this is not enough.

Increased Capacity for Work.—Almost all patients are able to go back to their previous jobs or are able to do some kind of gainful work. Some of the patients were completely incapacitated for work before operation, and others were not so incapacitated. With many a patient the anatomy in the heart is good and the anginal pain is comparable to an incapacitating toothache and the result of operation is comparable to that after extraction of the tooth. To be freed from incapaciting anginal pain is scarcely a figment of the patient's mind.

Cold Feet Before Operation; Warm Feet After Operation.—Many patients stated that their feet were warmer after operation. A study of foot temperatures was carried out.[4] Twenty-three patients were studied who had cold feet before operation. In 21 of these the temperatures after operation rose 4 to 5 C. The greatest rise was 10 C in one patient and 8 C in each of two others. If the temperatures were normal before operation, they remained normal after operation. What is the significance of warming of cold feet? First, this is an objective measurement which must be accepted as fact. Physiologically it means that the circulation to the feet is improved by operation on the heart; more blood has reached the feet. The mechanism is not known, but presumably it is by release of spasm.

Many patients state that the entire body is warmer. Some of the patients stated that their memory is improved and that they can comprehend conversation better. Releasing of cerebral spasm is not to be dismissed as an impossibility.

Absent Radial Pulse Before Operation and Return After Operation.—The radial pulse in the left arm disappeared when a patient had an occlusion of a coronary artery. Blood pressure could not be obtained in this arm, and the pulse was absent for one year when operation was done on the heart. Two days after operation it was noticed that the pulse was present and the blood pressure in the left arm was the same as in the right arm. The obvious explanation of this is that the disease produced arterial spasm of a large artery elsewhere in the body and that this spasm was released by operation on the heart. In terms of physiology it is significant, first, that this relationship existed and, second, that the surgical operation was effective in releasing it.

Irregularities of Heart Beat Before Operation; Disappearance After Operation.—In 20 patients operated on, chronic arrhythmia was the most prominent and important symptom before operation. These arrhythmias in most of these patients were distressing and alarming. In 17 patients the arrhythmias either completely disappeared or they diminished in frequency and severity after operation.[5] This is presented as objective evidence of benefit from operation.

Improvement in Ballistocardiogram After Operation.—Ballistocardiograms were done on 17 consecutive patients operated on. In 13 of these the record was abnormal; in 3 it was normal. Significant improvement in the record occurred after operation in 11 of the 13 patients who showed abnormal records before operation.[6] in two, the record did not change. The improvement in the ballistocardiogram indicates improved contractility of the myocardium. This study is presented as objective (not subjective) evidence of benefit from operation.

Summary and Conclusions

Blood supply to ischemic muscle is the primary consideration in the physiology and treatment of coronary heart disease. The relative effectiveness of glyceryl trinitrate and of surgical operation has been studied. The problem of treatment is selection of the most effective method for the three disease factors. These are electric imbalance, inflow reduction, and muscle destruction. The first of these yields to surgical treatment.

Results, including mortality, subjective improvement, and objective measurements, were studied in 347 consecutive patients. The fact that cold feet before operation become warm after operation indicates improved circulation in far away parts of the body. The physiology involved here deserves more than passing consideration. This objectivity together with the clinical results (plus a firm foundation from the laboratory) should help to prove that the operation is nothing less than an effective and beneficial procedure.

2065 Adelbert Rd. (6) (Dr. Beck).

This work was supported by grants from the United States Public Health Service and the Cleveland Area Heart Society.

Figures 1 and 2 are reproduced with permission from the *Journal of Thoracic Surgery* (36:329-351 [Sept.] 1958).

References

1. Beck, C. S., and Leighninger, D. S.: Operations for Coronary Artery Disease, J. A. M. A. 156:1226-1233 (Nov. 27) 1954; Scientific Basis for Surgical Treatment of Coronary Artery Disease, ibid. 159:1264-1271 (Nov. 26) 1955. Beck, C. S.: Coronary Artery Disease—Physiologic Concepts—Surgical Operation, Ann. Surg. 148:439-460 (April) 1957; Coronary Artery Disease: Report to William Harvey 300 Years Later, Am. J. Cardiol. 1:38-45 (Jan.) 1958; Coronary Heart Disease: Evaluation and Criticism of Present Day Concepts, editorial, ibid. 1:547-552 (May) 1958; Coronary Heart Disease: Three Dominant Causes of Death, Am. J. Surg. 95:743-751 (May) 1958.

2. Brofman, B. L., and Beck, C. S.: Coronary Heart Disease: Hemodynamic Principles and Their Therapeutic Applications, J. Thoracic Surg. 35:232-254 (Feb.) 1958.

3. Hahn, R. S., and Beck, C. S.: Revascularization of Heart: Study of Mortality and Infarcts Following Multiple Coronary Artery Ligation, Circulation 5:801-815 (June) 1952.

4. Baumgartner, D. A., and Nevin, J. E.: Changes in Peripheral Circulation in Lower Extremities Following Beck 1 Operation for Coronary Heart Disease, Am. J. Cardiology, to be published.

5. Brofman, B. L.; Bond, J. F.; and Leighninger, D.: Influence of Beck Operation on Chronic Arrhythmias Associated with Coronary Heart Disease, to be be published.

6. Brofman, B. L.; Arbeit, S. L.; and Adicoff, A.: Ballistrocardiographic Evaluation in Surgical Treatment of Coronary Heart Disease, Am. J. Cardiology, to be published.

YOUR MALPRACTICE INSURANCE CONTRACT

Howard Hassard, LL.B., San Francisco

Professional liability insurance does not cover all possible risks that are inherent in the practice of medicine. Even with high limits of coverage, medical society endorsement, or the assistance of a skilled broker, there may still be gaps in your contract. Accordingly, you must be aware of the major points to check before you buy.

Examination of Insurance Contract

The Insurance Carrier.—Know the other party to the contract: the insurance carrier. Some companies have a well-deserved reputation for liberal handling and not resorting to loopholes; others are noted for strict interpretation and resort to the fine print.

Seek companies that are well established and that have adequate reserves and unassigned surplus. A company with inadequate reserves or surplus may be inclined to seek loopholes if it faces a heavy loss and leave you, the physician, to face the plaintiff's lawyer alone and unprotected.

The insurance company should be subject to the laws of the state where you practice and subject to insurance department rules and regulations. In the

Read in the Session on Medical Professional Liability before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

Professional liability insurance contracts are not all the same. Individual contracts must be studied for possible gaps in coverage. The limitations and exclusions they contain are not a criticism of the insurance industry, for they determine whether an insurance company can stay in business. The physician should understand the insuring clause, monetary limits, exclusions, practice limitations, territorial limitations, settlement restrictions, the cancellation clause, and the extent of his duty to cooperate with the insurer. The basic reason for the need of cooperation is that the insurance carrier assumes a substantial monetary risk and, in return for it, is entitled not only to a premium but also to full and honest assistance from the insured physician. The gravest error is to purchase on the basis of price alone. Physicians should examine their current professional liability policies with these facts in mind.

event of a suit over the policy provisions or activities of the company, the state insurance department can be of material assistance without cost to the insured.

It is essential in the field of malpractice liability, because of latent liabilities, that the company not only has financial stability but has been in business long enough so that it can be reasonably expected to continue in business in the foreseeable future.

Differentiation of Terms.—Know what your contract with the insurance company contains and does not contain. Know the differences between company, broker, and agent:

The Company: A company or insurance carrier is the entity, usually a corporation, which is financially obligated under the insurance contract to carry out the provisions of the policy and to assume the defense and expense of any claims brought against the assured under the policy.

The Broker: A broker is one who is licensed to transact the business of insurance and who represents the buyer. He may place his business with any company, and in so doing he remains the agent of the buyer. You may look only to your broker and no one else in the event he fails to remit your premium to the company, secures improper coverage, or carelessly handles your needs.

The Agent: An agent is one who is licensed by an insurance company to transact the business of insurance. He represents the company which licenses him, and he binds that company by agency. In this instance, responsibility is in both the agent and the insurance company. A person may be both a broker and an agent, but generally he is one or the other.

The Underwriter: Another term frequently used is "underwriter." Legally, this means an insurer or company, but some brokers adopt the term as part of a trade name. This practice is confusing, and one must be alert to the fact that underwriter may only signify a broker.

What Malpractice Policies Contain

You should know what is in your policy and how it works. Malpractice policies contain these subjects: (1) insuring clause, (2) monetary limits, (3) exclusions, (4) practice limitations, (5) territorial limitations, (6) settlement restrictions, (7) cancellation clause, and (8) provision for duty to cooperate with the insurer at all times.

The Insuring Clause.—The insuring clause in the contract defines types of claims covered. There is no uniformity in this field—unlike, for example, fire and life insurance. The usual insuring clause, which reads "injury arising out of malpractice, error, or mistake in rendering or failing to render professional services," should be carefully analyzed. It may not cover assault, battery, breach of implied contract, libel and slander, and agreements guaranteeing the result of treatment, to specify some of the nonerror types of claim. You should read your contract carefully, with these questions in mind:

First, does your policy contain a provision to defend all claims and suits, including malicious prosecution, counterclaims and cross-complaints (which arise when suing to collect fees), and suits based on failure to act (omission), i. e., services you "should have rendered"?

Second, do you have coverage for personal restraint? This means false imprisonment (for instance, a claim may arise when helping a family cope with an acute psychiatric emergency).

Third, do you have coverage for undue familiarity? Take precautions; take your nurse on calls, and never examine alone if you have reason for suspicion.

Fourth, does your policy include coverage for assault and battery? Four per cent of all suits against physicians are not based on alleged malpractice but are predicated on a claim of assault and battery. Generally, such suits claim the surgeon operated without proper consent or went beyond consent given.

Fifth, what about implied contracts? You may be sued for breach of contract if your patient interprets your prognosis as a guarantee he will get well. Say nothing that will be interpreted as a promise to cure. Suing for breach of contract has become popular of late among plaintiffs' lawyers. It gets around necessity for an expert witness, but, also, it gets around your insurance unless your policy expressly covers contract claims.

Sixth, does your policy cover you in case of charge of libel or slander? A patient may claim violation of your duty to remain silent. The California Medical Practice Act states that willful betrayal of a professional secret is ground for revocation of license; it can also be the basis for a slander suit. Say or write nothing that will violate the privilege.

Seventh, is premise liability coverage included? This is important if you are the owner or lessee of premises. Sometimes it is difficult to determine whether a suit is for alleged malpractice or for premise liability—as when a patient falls in a treatment room. Use the same company for malpractice and premise liability. Split liability can involve a conflict between carriers and shifting of responsibility, e. g., a patient under narcotics slips on tile in waiting room—which policy covers it?

Before leaving the subject of scope of coverage, I cannot resist recounting an unusual happening. A doctor, while performing an orthopedic procedure in a hospital, caused the instrument to slip, badly injuring his physician assistant. The question was what insurance would protect the doctor from a claim or suit by the assisting physician?

His malpractice insurance actually did not apply, because this accident was not covered under the insuring clause which only covered injuries to patients while rendering professional services. His comprehensive personal liability did not apply, as professional services or business activities were excluded. His premise liability policy did not apply,

as it was unrelated to the insured premises (i. e., his office). The hospital insurance did not apply, for it did not involve defective equipment. The doctor was completely dependent on a superliberal interpretation of his malpractice contract to cover the claim.

Monetary Limits.—How much insurance coverage do you have? Are your total limits measured by occurrence of accident or aggregate?

Are legal expenses included? With today's verdicts, $100,000-per-$300,000 coverage does not go very far. In California there have been several jury verdicts over $200,000 and at least one settlement before trial in excess of $250,000.

Exclusions.—Read your policy to be on guard as to what is not covered. The exclusions are usually plainly and unequivocally stated.

Are other people in your office covered? These include nurses, assistants, employees, and substitutes or *locum tenens*. I know it is not nice to mention it, but if a physician employs a "ghost" surgeon he may be uninsured, because some policies require the specific consent of the patient to the operator as well as to the operation. Also, are your partners insured? Suppose you are individually insured, and your partner is being sued and he dies; you are responsible for his acts as partner. Are you covered? It is wise to have partners covered in the same company and as partners, as well as individually.

Some of the routine exclusions are as follows:

First, intoxication and drugs, the exclusion for which usually reads, "shall not pay . . . in suits based on services rendered while under the influence of intoxicants or drugs."

If you leave a cocktail party to answer an emergency call, are you covered? If you took barbiturates at bedtime and answered an emergency call, are you covered?

If your contract excludes acts or omissions "while under the influence of drugs or alcohol," strictly speaking you are not covered for damages if an "under the influence" charge is made and can be proved. "Under the influence" or "drunk" are not well-defined phrases. Different courts define both terms in different ways. "Under the influence" is a relative term embracing various degrees of intoxication and mental obscuration. Here are a few sample definitions:

> This condition presents various degrees of intensity, ranging from a simple exhilaration to a state of utter unconsciousness and insensibility. (*Paris v. Robinson*, 140 S. W. 434)
>
> The condition of a man whose mind is affected by the immediate use of intoxicating drinks. . . . Under the influence of intoxicating liquor to such an extent as to have lost the normal control of one's body and mental faculties, and, commonly, to evince a disposition to violence, quarrelsomeness and bestiality. (*Zee v. Gary*, 189 So. 34)
>
> When one's brain is so far affected by potations of liquor that his intelligence, sense perception, judgment, continuity of thought, or of ideas, speech, and coordination of volition with muscular action are impaired or are not under normal control. (*Wilson v. Inter-Ocean Cas. Co.*, 188 S. E. 102)

Second, unlawful or criminal acts are invariably excluded. Is this limited to acts you know to be wrong? What about innocent acts, or what if you are forced to take unlawful action by an emergency or physical compulsion of another?

What is an unlawful act? Is it any infraction, no matter how minor, or must it be a felony or a serious misdemeanor? Is the word "unlawful" synonymous with "criminal"?

How directly must the unlawful act be connected? An illegal abortion is clearly not covered, but how about plastic surgery on a criminal? Or, what if you employ an unlicensed person in your office? In one California case, years ago, the insurer denied liability in a case against a partnership of radiologists because they had employed a well-trained radiologist from Canada who was not yet licensed in California. The insurer said employment of unlicensed physicians is unlawful, we exclude unlawful acts, good bye.

Is all coverage lost by violation of this condition? Under one form of contract the physician loses both his defense costs and indemnity in the event a suit against him falls within the "unlawful acts" exclusion. Under another form of contract the insurance company must still defend the physician, even though unlawful acts are charged or found, but the physician is obligated to pay any judgment rendered against him.

It is essential that each physician know the effect of each and all of the exclusion clauses in his malpractice contract.

Practice Limitations.—There are two types of practice limitation found in malpractice insurance contracts. One type is an outright exclusion of certain procedures, e. g., fluoroscopy and anesthesia, unless a special added premium is paid; the other type is a classification of practice for determining a basic premium rate, i. e., general practice versus surgery.

Frequently, the application for insurance that must be signed in order to obtain a contract contains representations by the physician as to the scope and type of his practice. These representations may or may not be "warranties." If the application form becomes a part of the contract or uses language to the effect that the insurer may rely on the representations as warranties, it is possible that a mistake or omission by the physician in filling out the application form can result in a denial of liability by the insurer, if a claim arises. It is essential, therefore, that each physician carefully read and accurately answer the application, particularly those questions relating to the scope and type of practice, as well as questions relating to prior claims or suits.

The usual practice limitations found are anesthesiology, therapeutic radiology, and fluoroscopy. The usual basic premium rate differentials are between 100% nonsurgery, some surgery, and exclusively a surgical practice.

As long as the word "surgery" is understood, classification for rating purposes by the physician is not difficult. However, surgery may be defined differently in different insurance contracts. One contract, for example, defines both major surgery and minor surgery. Another contract classifies everything that involves puncturing, penetrating, or severing tissue as surgery.

Incidentally, the contract that classifies major surgery and minor surgery for rate purposes distinguishes between major and minor by listing specific procedures under each category. The physician must carefully read the entire list in order to be certain that he properly classifies himself.

Territorial Limitations.—Many malpractice insurance contracts exclude coverage while the insured is outside the United States and its territories. Some policies include Canada, but no other foreign country. If you travel abroad be sure and check your malpractice contract in advance, because even emergency treatment rendered outside the United States could result in a lawsuit for which you would be uninsured.

Settlement Restrictions.—Most professional liability insurance contracts provide that the insurance company may not settle a claim or suit without the consent of the insured physician. This is a most important provision for the protection of the physician. Inasmuch as professional liability claims involve professional reputations as well as money, it is of paramount interest to the insured physician that he have control over the disposition of a claim made against him. Some professional liability contracts omit this provision and allow the insurance carrier to settle claims without the consent of the physician. A few contracts contain a built-in booby trap; it is this:

The contract contains the usual provision that settlement may not be made without the consent of the insured physician, but then a sentence follows providing that, if the physician refuses to approve a settlement offer and the case is then tried and lost, the insurance coverage is automatically limited to the amount of the settlement offer. In other words, a physician may refuse to settle, but if he does so he acts at his own risk and automatically reduces the amount of his coverage to the amount of the tendered settlement.

Cancellation Clauses.—Practically all professional liability insurance contracts permit either party to cancel at any time; usually 10 or 30 days' written notice of intent to cancel is required. A few group programs have protection against wholesale cancellation by agreement with the group carrier; however, this is the exception rather than the rule. Most physicians in the United States are currently insured for professional liability under contracts that can be canceled in not more than 30 days.

Duty to Cooperate with Insurer.—The typical professional liability policy contains the following clause: "The insured shall cooperate with the company, and, on the company's request, shall attend hearings and trials and shall assist in effecting settlements, securing and giving evidence, obtaining the attendance of witnesses, and in the conduct of suits. . . . The insured shall not voluntarily make any payment, assume any obligation, or incur any expense at his own cost, without the consent of the company previously given in writing."

Various contracts will use variations of the foregoing language, but all in effect require the insured physician to cooperate with the insurer in the defense of any claim or suit.

Cooperation includes prompt notice to the insurance carrier whenever an incident occurs that could give rise to a liability claim; cooperation requires that the insured physician not undertake to handle the matter himself; and cooperation requires that the physician not "build" a claim in conjunction with his patient for the purpose of securing compensation from the insurance carrier. Such activity can result in the insurance carrier denying liability because of the physician's breach of the cooperation clause.

The basic reason for the contract provisions requiring that the physician cooperate with and assist his insurer is that the insurance carrier assumes a substantial monetary risk, and in return for this risk it is entitled not only to a premium but also to full and honest help and assistance from the insured physician.

Another facet of the cooperation clause is the usual contract provision that the insured physician shall neither admit liability nor attempt to make a settlement on his own account. It is most important to remember that in all liability insurance contracts the insured has no right to give away the insurer's money.

Comment

Professional liability insurance contracts are not all the same. They differ in many respects and are almost as individualistic as women's hats. It is never safe to purchase professional liability coverage without reading and understanding the contract, on the assumption that it will protect you no matter what happens. In fact, even the broadest professional liability policy contains exclusions and limitations. Have your policy provisions interpreted by a person experienced in professional liability insurance who can relate the insurance clauses to the practice of medicine. Few people in the insurance business or in the legal profession have had sufficient experience in the medical malpractice field to properly apply policy terms to a medical practice.

For example, assault and battery is generally interpreted as a physical assault, whereas in malpractice it is, in addition, interpreted to include failure to obtain a proper consent to a treatment or operation or failure to inform a patient of any change in the original scope of the surgery to be performed.

The gravest error is to purchase on the basis of price alone. When a physician is threatened with a professional liability suit, he desperately needs the aid and assistance of expert claims adjusters and counsel—to say nothing of the need to protect his property. The penny-wise pound-foolish purchaser who bought the cheapest contract and did not read it may discover when his need arises that he is not covered; or he may find that he is covered but has a contract that permits the insurance carrier to compromise or settle without his consent or that he has a contract with a five-day cancellation clause which is immediately exercised.

The fact that professional liability insurance contracts contain exclusions and limitations is not a criticism of the insurance industry. An insurance company to stay in business must at least break even; no business can survive for long if it pays out more than it takes in. The insurance business is highly competitive; the purchasers of insurance pick and choose; and when the buyers want price economies the insurance carriers have no choice—to stay in business they must compete price-wise, and to compete price-wise they must limit their liability. No one can change this basic law of economics.

Conclusions

I hope that this paper may stimulate those physicians who hear or read it to examine their current professional liability policies, and to determine—through inquiry to their carriers if necessary—the acts or omissions for which they are covered or not covered, and the limitations and other provisions that may take away coverage if the physician's behavior is contrary to the contractual commitment. It is better to know in advance than to find out after it is too late.

111 Sutter St. (4).

EXPERT WITNESS AND ADVISORY PANELS

Joseph F. Sadusk Jr., M.D., Oakland, Calif.

The difficulty involved in obtaining expert medical testimony from physicians in personal injury cases is well known. It is due not to his unwillingness to cooperate with the law but rather to the fact that he is cast into an atmosphere foreign to his training and philosophy. The physician is trained as a scientist to present medical data and conclusions in a narrative and factual manner and to elaborate on the pros and cons of the medical problem. Due to the adversary system of trial in the United States, this is not generally possible. Under such a system, the physician replies to a series of questions which, when put by an experienced trial attorney, may modify, twist, and distort the true medical story.

A milestone was reached in 1952 when the justices of the Supreme Court of the County of New York encouraged the local bar associations and medical societies to embark on a system for impartial medical testimony in personal injury cases.[1] The success of this project led to a permanent continuation of the procedure, and similar or identical plans will doubtless appear in other parts of the United States.

Except for an initial pilot plan pioneered by the Los Angeles County medical and bar associations several years ago, there has been little or no at-

It is difficult to obtain expert medical testimony from physicians in personal injury cases. This is not due to unwillingness to cooperate with the law but rather to the fact that the physician is cast into an atmosphere foreign to his training and philosophy. A plan has been formulated to make available a panel of physicians for consultation with attorneys of the local or neighboring bar associations for presuit expert opinion and, where suit is instituted, for testimony as an expert witness. The education of physicians to serve on these professional liability medical panels is considered of paramount importance. This is accomplished through a thorough indoctrination by a joint committee of the local medical and bar associations, with or without the assistance of special statewide indoctrination committees where such assistance is considered desirable and necessary by the local working units. The success of these panels will depend on the professional qualifications and impartiality of the panel physicians and the willingness and readiness of attorneys to accept a neutral and unbiased opinion.

Member, Committee on Medicolegal Problems, American Medical Association.

Read in the Session on Medical Professional Liability before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

tempt to solve the problems of expert medical advice and testimony in the field of medical malpractice, a small but nevertheless important segment of personal injury litigation. Here the natural disinclination for the physician to testify is compounded by the fact that he must advise and testify against a colleague—a fellow physician—whom he may see week in and week out. Such reluctance is natural and understandable. The law and organized medicine have long been aware of this problem, but it remained for the California Medical Association and the State Bar of California to simultaneously agree to investigate and confer on the solution of the availability of impartial medical expert witnesses in alleged medical malpractice cases.

As a result of the 1955 meeting of the Conference of California State Bar Delegates, a committee was appointed to study the problem of obtaining evidence in malpractice cases. Meetings were held with representatives of the California Medical Association to explore the situation, after which the Board of Governors of the California State Bar and the Council of the California Medical Association appointed comparable committees to meet in joint session to formulate a plan which would make available to attorneys the services of qualified physicians to advise on a case of alleged malpractice and, if suit were instituted, to testify as an expert witness. In September, 1957, these committees recommended to their respective parent organizations the plan presented here.[2]

The Plan

The purpose of the plan is to form a panel of physicians available for consultation with attorneys of the local or neighboring bar associations for pre-suit expert opinion and, where suit is instituted, for testimony as an expert witness. Such a panel would be used only for cases of alleged medical malpractice.

Selection of panels would be on an appointment basis by the medical societies within each territorial district, with approval of the panel by the board of directors of the applicable local county bar association.

Disqualification of a panel member would occur if he is treating or has ever treated or consulted on the plaintiff patient or if there is a relationship, business or otherwise, between the panel member and the defendant physician.

The panels would include members from general practice, from the following basic specialty areas of medical malpractice, and from such additional areas of specialty practice as shall be determined within each district: (1) medicine, (2) surgery, (3) obstetrics and gynecology, (4) pediatrics, (5) pathology, and (6) radiology.

Administration of a panel would be by a designated officer of the local county bar association, with names on file.

A panel member would be called by the complainant's request in writing to a physician on a panel list as submitted by the local bar association. The physician then notifies his county medical society and the local bar association in writing of the requested consultation, giving name of attorney, complainant, and physician complained against.

Education of a panel would be accomplished by a series of lectures from a joint committee of local medical and bar association members or by special statewide indoctrination committees.

For the consultation and examination, review of records, preparation of report, and testimony, the physician receives the reasonable value of his time in accordance with the prevailing fees in his community.

No reference may be made in court to the panel or medical or bar associations' participation therein. Judges are requested to adopt a rule forbidding counsel (on each side) to mention the status of the witness in relation to the panel.

A panel physician who consults with or examines a complainant may not, without the consent of the complainant, be examined in a civil action as to any information acquired from the complainant which was necessary to enable the physician to prescribe or act for the complainant, except as provided below.

A complainant may secure additional examinations or consultations from the panel list, but only if the complainant agrees in writing, with the preceding panelist consulted, that the latter may be examined in any civil action based on the complaints involved.

A complainant may secure an examination or consultation with a second member of the over-all panel without being required to waive the confidential nature of the first examination or consultation, providing the initial panelist selected reports in writing to the administrative officer of the local county bar association that the complaint is not within his area of practice or that a second examination or consultation is necessary or advisable for the stated cause.

The "Ground Rules" of the Plan

This plan was approved by the governing bodies of the parent organizations in September, 1957. The committees then met again to outline and to recommend certain "ground rules" to the individual medical societies and county bar associations of California, at which level the plan was to be implemented. Further, it was made clear that these working units were free to modify the plan to meet local conditions and attitudes and, indeed, the local county and bar units were free to accept or reject the entire concept of such panels. These basic "ground rules" were as follows:

Panel members are to be appointed by the county society, not selected from volunteers. Only those panel appointees who have attended the in-

doctrination lectures are eligible to serve. Present members of public service or malpractice committees of county societies are not eligible for service on the panel. Panel appointments are for one year only; a new panel is appointed each year, but the same physicians are eligible year after year. Panel members, as such, are available to complainants against doctors of medicine only. In each county, the panel should be representative of the practice of medicine in that area as to specialties and general practitioners. The financial arrangements between the complainant's attorney and the panel member are to be by agreement between them, although a fee scale may be established by the county medical society if it so desires. Fees are to be paid in advance unless otherwise agreed between the panel member and the attorney.

Specific Instructions for the Physician

The education of physicians to serve on these professional liability medical panels was considered of paramount importance, to be accomplished through a thorough indoctrination by a joint committee of the local medical and bar associations, with or without the assistance of special statewide indoctrination committees where such assistance is considered desirable and necessary by the local working units. Specific instructions are to be sent to each physician panel member with his obligations clearly outlined along the following lines.

Notification of State and County Bar and Medical Associations.—The physician will be instructed to immediately notify the respective organizations by completion of a special form in quintuplicate, of which he will retain one copy and mail the remaining four copies to the California Medical Association. This organization will assume the responsibility for distribution of the copies to the county bar and medical associations and to the California State Bar. This notification is considered necessary to insure the adherence of attorneys to the rule of the formulated plan which provides for written waivers by the complainant or his attorney when securing additional medical opinions from the panel. In addition, these reports will insure that the panel member's rights will be protected by the bar and medical associations. Further, analyses will be made as the years go along to evaluate and to improve the program.

Instructions for Thorough Study of All Medical Factors.—The necessity for a thorough and impartial review of the case before the physician expresses an opinion is to be emphasized to the physician, wherein he is to examine the patient, and to review all available evidence including hospital records, x-rays, laboratory reports, and other medical records and data which can reasonably be obtained before rendering a report.

Report of Opinion and Testimony.—The physician will be required to submit his report to the plaintiff's attorney in writing covering history of the injury, the patient's account for treatment and its results, findings on examination of the injured part or parts and notation of abnormalities, indications if another field of medicine outside the physician's field is involved, the extent of injuries and conclusions as to degree of disability, and, finally, an opinion as to whether or not the defendant doctor deviated from the legal requirement of "standard and accepted medical practice." It will be the physician's duty to testify in court as to his opinion if the case goes to trial.

Objective and Impartial Attitude.—The physician will be advised to not become an advocate for either side but rather to evaluate the facts objectively and render an impartial opinion.

Promptness in Rendering Reports.—The physician will be impressed by the fact that undue delay in reporting to the plaintiff's attorney may prejudice the interests of either or both the complainant and the doctor complained against.

Disqualification of Panel Physician.—The panel physician is to be disqualified if (1) he has treated or is treating the complaining patient or has been consulted by representatives of the physician, (2) there are personal or other relations with the patient which might prejudice the physician's opinion, (3) there is a business or a personal relationship between the panel physician and the defendant physician which would make it impossible to render an impartial opinion, (4) the medical problem is not within the field of practice of the panel physician, and (5) the nature of the case or other commitments would make it impossible for the physician to devote the time necessary for a full study of the case.

Comment

It is to be emphasized that this plan for a professional liability medical panel has not yet reached the working stage. These panels are presently being set up throughout the major population areas of California where agreed to by both local county medical and bar associations. Modifications and changes will doubtless be required as time goes along with experience gained by attorneys and physicians in the use of the panel.

The success of these panels will depend on the professional qualifications and impartiality of the panel physicians and the willingness and readiness of attorneys to accept a neutral and unbiased opinion. That organized medicine and the law has reached such an agreement speaks for the willingness of both parties to serve the administration of justice.

459 30th St. (9).

References

1. Special Committee of the Association of the Bar of the City of New York: Impartial Medical Testimony, New York, the Macmillan Company, 1956.

2. West, F. E., and Archer, J. W.: Medical Expert Panels for Malpractice Cases, California Med. 88:173-175 (Feb.) 1958.

CLINICAL NOTES

ASYSTOLE COMPLICATING ACUTE MYOCARDIAL INFARCTION

SURVIVAL WITH THE AID OF A CARDIAC PACEMAKER AND INTRAVENOUS ADMINISTRATION OF ISOPROTERENOL

Sylvan D. Solarz, M.D., David M. Berkson, M.D.
and
Alfred Pick, M.D., Chicago

Since the development by Zoll [1] of an external cardiac pacemaker capable of producing effective ventricular contractions by transthoracic electric stimulation many cases of asystole have been successfully treated with the aid of this device alone or in combination with intravenous administration of isoproterenol (Isuprel) hydrochloride.[2] The majority of the reported cases have been those of chronic atrioventricular block with Stokes-Adams disease. Recently we had opportunity to apply this regimen to a patient in whom an advanced second degree atrioventricular block with Stokes-Adams attacks developed acutely in the course of a myocardial infarct. (The term "advanced second degree atrioventricular block" is applied to cases in which several successively dropped beats initiate atrioventricular nodal escape and dissociation with or without ventricular captures.[3]) To our knowledge this is the first such case with survival treated in this manner. Continuous monitoring of the rapidly changing cardiac mechanism in conjunction with automatic release of the pacemaker when needed permitted prompt adjustments of the therapy according to instantaneous needs and an immediate evaluation of the effect each new procedure had on the cardiac rhythm. We used a unit consisting of an external cardiac pacemaker, a cardiac monitor with both visual and auditory signals of each ventricular beat, and a cardioscope with continuous display of an electrocardiographic tracing. After a predetermined asystolic period the pacemaker automatically goes into action, and an alarm is sounded. External electric impulses continue at a preselected rate and strength until the machine is turned off manually. This type of action serves to bring instant attention to the patient and to shorten the period of asystole.

Report of a Case

A 58-year-old female was admitted to Michael Reese Hospital on May 8, 1958, with the complaint of severe substernal pain. The patient had been under the care of one of us (S.D.S.) for five years because of coronary heart disease with anginal syndrome and congestive heart failure. She had been well maintained on therapy with digoxin (Lanoxin), chlorothiazide (Diuril), and glyceryl trinitrate. Previous electrocardiograms (fig. 1, 1953) were relatively stable over the years and showed a first-degree atrioventricular and a right bundle-branch system block without evidence of myocardial infarction. The evening prior to admission the patient experienced substernal pain relieved by glyceryl trinitrate; however, later that night she was awakened from her sleep by severe chest pain requiring narcotics for relief.

On admission the pertinent physical findings were as follows: pulse 84 beats per minute and regular; blood pressure 140/70 mm. Hg bilaterally; thyroid gland slightly enlarged to palpation; the lungs clear; the heart size normal; the second aortic sound of normal intensity and louder than the second pulmonic sound; a grade 1 systolic murmur heard over the base of the heart; the liver not palpable and no signs of congestion.

Admission laboratory data included the following findings: hemoglobin level 13.4 Gm.; white blood cell count, 21,300 per cubic millimeter, with 85% polymorphonuclear cells, 11% lymphocytes, and 4% monocytes; sedimentation rate, 17 mm. per hour (Wintrobe); fasting blood sugar level, 168 mg.%; serum urea nitrogen level, 28 mg.%. The serum transaminase on May 8 was 24 units, and on May 9 it had risen to 73 units. The electrocardiogram (fig. 1, 5-8-58) revealed, as previously, sinus rhythm with first-degree atrioventricular and right bundle-branch system block and, in addition, contour changes characteristic of acute posterior wall infarction. Initial therapy included bed rest, oxygen tent, anticoagulation with heparin and warfarin (Coumadin), and digoxin.

The patient did well for the first 24 hours. On May 9 an intermittent pulsus bigeminus was noted, and another electrocardiogram was taken. This showed sinus rhythm with incomplete atrioventricular dissociation due to a second-degree atrioventricular block with repetitive nodal escapes (fig. 2, 5-9) and further contour changes suggesting extension of the infarction to the lateral wall. The average ventricular rate was 60 per minute, and the blood pressure was unchanged. The patient remained in good clinical condition, and on the following day the heart rate was regular. On May 11 a pericardial friction rub was noted, and shortly thereafter the blood pressure fell precipitously, moist rales and hepatomegaly developed, and the clinical condition deteriorated rapidly. An intravenous infusion of arterenol, 2 ampuls (16 mg.) in 1,000 cc. of 5% dextrose in water, was started immediately, and the patient received additional digitalis and a mercurial diuretic. The blood pressure promptly rose to satisfactory levels. An electrocardiogram (fig. 2,

From the Department of Medicine and the Cardiovascular Department of the Medical Research Institute, Michael Reese Hospital.

5-11) revealed irregularity and marked slowing of the ventricular rate to an average of 35 per minute due to a more advanced atrioventricular block with a complex mechanism [4] and signs of continued extension of the infarction. On May 12, because of a persistent slow ventricular rate, isoproterenol therapy, 10 mg. sublingually every four hours, was started. In spite of this there were several momentary lapses of consciousness, and the isoproterenol dosage was increased to 15 mg. On this medication the ventricular rate rose to 50 and became almost regular. An electrocardiogram (fig. 2, 5-12) showed sinus rhythm with a 2:1 atrioventricular block, alternating with periods of atrioventricular dissociation during which an accelerated ventricular pacemaker operated at about half the sinus rate. However, on the morning of May 13, an episode of ventricular asystole with convulsions and cyanosis occurred, and the patient appeared moribund. After vigorous pounding of the precordium the heart resumed beating. Isoproterenol, 0.2 mg., was given intramuscularly immediately, and the automatic external pacemaker was attached to the patient with the release time set at three seconds of asystole. The isoproterenol injection was repeated within the next hour but failed to prevent frequent periods of ventricular standstill. Each asystole brought the automatic pacemaker into action, with prompt restoration of spontaneous heart beats. A constant intravenous drip of isoproterenol was then begun, with 2 mg. per 500 cc. of 5% dextrose in water at an initial rate of 15-20 drops per minute corresponding to approximately 4 mcg. per minute.[2] After several periods of asystole leading to pacemaker discharge, it was found that 60 volts was adequate to produce ventricular contractions. Electrocardiograms between asystolic periods (fig. 3, *upper strip*) showed an irregular ventricular rate because of atrioventricular conduction ratios varying between 2:1 and 5:1, with ventricular escapes terminating those pauses which were not long enough to bring the external pacemaker into action. One of the longer ventricular pauses, with nine successively blocked P waves, leading to automatic discharge of the pacemaker and subsequent resumption of the original mechanism, is illustrated in the lower strip of figure 3.

From May 13 until the afternoon of May 15 the patient was kept on the regimen of treatment with intravenously given isoproterenol with the pacemaker constantly attached to the chest. During this period the predominant rhythm was a second-degree atrioventricular block with varying atrio-

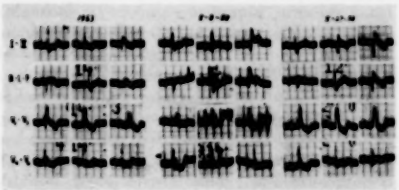


Fig. 1.—Three 12-lead electrocardiograms showing development (*1958*) of characteristic features of posterolateral wall infarction on top of a preexistent right bundle-branch system block (*1953*).

ventricular ratios. As the rate of the infusion was slowed, ventricular pauses became longer and caused discharge of the pacemaker. As the infusion rate was increased, shorter ventricular pauses were terminated by nodal or ventricular escapes, but in addition several brief paroxysms of auricular fibrillation and of ventricular tachycardia were observed on the cardioscope early on May 13 (fig. 2, 5-13). Late that evening it was noted that the ventricular rate was slowing and numerous episodes of asystole occurred requiring pacemaker stimulation. It was necessary to increase the voltage and the number of successive shocks to overcome the periods of ventricular standstill. Increase in the rate of flow of isoproterenol failed to prevent ventricular pauses, but bizarre ven-

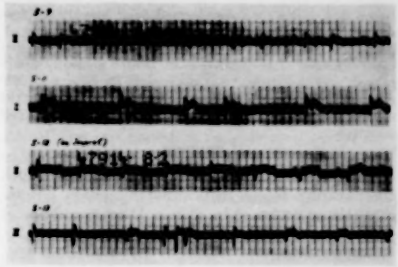


Fig. 2.—Electrocardiograms representative of variety of mechanisms encountered: Intermittent ventricular bigeminy as result of second-degree atrioventricular block with nodal escapes (5-9). Marked slowing of ventricular rate as result of more advanced atrioventricular block (5-11). Consequent to isoproterenol (Isuprel) medication, 2:1 atrioventricular conduction changing to atrioventricular dissociation with accelerated ventricular pacemaker (5-12). Paroxysm of auricular fibrillation with complete atrioventricular dissociation, alternating nodal and ventricular pacemakers, and short burst of ventricular tachycardia (5-13).

tricular complexes of variable contour appeared, progressively increasing in frequency, and eventually a continuous ventricular tachycardia developed. After five minutes of this rhythm the patient appeared moribund. At this point it was decided to replace the isoproterenol infusion by procainamide (Pronestyl) hydrochloride in an attempt to convert the rhythm; 50 mg. was given cautiously. This caused slowing of the ventricular rate and reappearance of a few supraventricular beats. The administration of an additional 75 mg. led to a ventricular standstill. Repeated shocking by the external pacemaker caused resumption of the original supraventricular rhythm, and the isoproterenol infusion was restarted at a reduced rate of flow. Several minutes later, paroxysmal ventricular tachycardia again appeared. It was stopped by another 100 mg. of procainamide which was followed by protracted ventricular arrest and then restitution of intrinsic ventricular activity by external electric stimulation.

Because of this difficulty in controlling the rhythm, the concentration of isoproterenol was changed to 2 mg. per 750 cc. of 5% dextrose in water. In addition, on May 14, the arterenol infusion was discontinued. Throughout this day and thereafter the blood pressure remained constant. There were several episodes of asystole promptly terminated by the external pacemaker, and in the afternoon the rhythm became stabilized with second-degree atrioventricular block and spontaneous nodal or ventricular escapes. On the afternoon of May 15, the atrial action changed from sinus rhythm to fibrillation but the average ventricular rate remained 40. Slowing or speeding up of the isoproterenol infusion altered neither the atrial mechanism nor the ventricular rate. It was

decided to stop the infusion to determine whether the ventricular rate would be maintained spontaneously. At first ectopic ventricular beats increased in frequency, and after 15 minutes asystole occurred long enough to cause discharge of the external pacemaker. Immediately after this, the auricular fibrillation reverted to sinus rhythm with second-degree atrioventricular block and a constant ventricular rate of 40. This was the last episode of asystole requiring external stimulation. On May 16 the atrioventricular block varied between first and second degree, and from May 17 on first-degree atrioventricular block became permanent (fig. 1, 5-27-58). The remainder of the hospital course was uneventful, signs of congestive heart failure gradually disappeared, and the patient was discharged on June 29, 1958. At the time of writing (August, 1958) she is following the usual course of recovery from a myocardial infarction of this severity.

Comment

The prognosis of advanced atrioventricular block complicating recent myocardial infarction has recently been reviewed by Cohen, Doctor, and one of us.[5] They found the over-all immediate (two-month) mortality in a series of 68 cases to be 47%, the death rate increasing with the severity of the block. Posterior wall infarcts accounted for 75% and carried an immediate mortality of 37%, whereas in anterior wall infarcts 75% of patients died. In

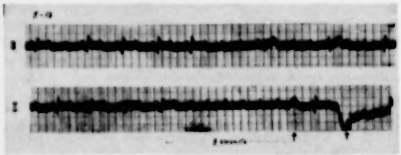


Fig. 3.—Consecutive portions of long record showing termination of ventricular pause by spontaneous ventricular escape (*upper strip*) and longer pause terminated by two automatic discharges of external pacemaker (*arrows*) initiating intrinsic ventricular impulse formation (*lower strip*).

32 of 36 surviving cases, atrioventricular block was transient. The long-term prognosis of those surviving the first two months was not affected by the temporary conduction disturbance. Therefore, it appears that if a patient survives the initial complication of atrioventricular block his chances for long-term survival are as good as those of one with an uncomplicated myocardial infarction. From an anatomic viewpoint it would appear that patients with a transient block have ischemia or edema involving the conduction system whereas actual necrosis of these tissues is present in cases with permanent conduction defects. From the clinical standpoint one cannot distinguish between these two possibilities during the acute episode, the time when adequate therapy is of the utmost importance. It is in line with this that recently the successful use of adrenal steroids in cases of acute myocardial infarction with Stokes-Adams attacks has been reported.[6]

While it is realized that each case of this nature requires individual measures which might not be applicable to others, in our case it is believed that the recovery is to be attributed not to a single agent or medication but rather to the awareness of impending attacks of asystole, to the proper preparations for handling such an event, and to the alertness of the members of the house staff assigned to this case.

The appearance of a bigeminal rhythm on auscultation early in the course of the patient's illness first brought to mind the possibility of second-degree atrioventricular block with 3:2 conduction. It has been our experience that bigeminy occurring in the course of acute posterior wall infarction is more often due to this latter mechanism than to ectopic impulse formation.[3] The electrocardiographic confirmation of the atrioventricular conduction disturbance alerted us to the possibility of its progression to Stokes-Adams attacks, although there was no clinical evidence of this at that time. As the degree of block increased isoproterenol medication was started sublingually, and the external pacemaker was kept nearby, ready for immediate use.

In order to maintain spontaneous intrinsic ventricular activity we had the choice of three sympathomimetic drugs: arterenol, epinephrine, and isoproterenol. At the time of the first syncope, the patient had been receiving arterenol intravenously constantly for about 48 hours and at that time was unable to maintain her blood pressure without it. The fact that such attacks occurred while the patient was receiving this drug is in keeping with its known pharmacological effects which do not include enhancement of nodal or ventricular pacemaker action. With regard to the two other agents, it has been found by Zoll and his co-workers[4] in comparative studies that, in patients with high blood pressure, isoproterenol might be preferable to epinephrine since it has no vasopressor action. On the other hand, epinephrine is the drug of choice when the pressure is normal or low. Furthermore, they state that epinephrine should be used in patients who, prior to the attacks, had functioning atrioventricular conduction "since it is a much less potent accelerator of the sinoatrial pacemaker than is isoproterenol and there is, accordingly, less risk of a rapid ventricular rate should atrioventricular conduction return." In our patient, however, the blood pressure had to be maintained artificially and it was felt that this should be done independently of the attempt to control ventricular activity. We were aware of the fact that the amount of the drug determining the ventricular rate might have to be varied from moment to moment and thus new problems might arise should control of blood pres-

sure and ventricular activity depend on the same medication. For this reason isoproterenol and arterenol were used simultaneously.

After the first convulsion, the isoproterenol medication was changed from sublingual to intramuscular administration and the automatic external pacemaker was attached to the patient. This arrangement prevented the occurrence of further seizures, but it soon also revealed that isoproterenol per se was inadequate to prevent protracted periods of asystole, even after its administration by continuous intravenous drip. On the other hand, the continuous infusion of isoproterenol probably was responsible for the prompt resumption of spontaneous ventricular activity after one or two external electric shocks (fig. 3, *lower strip*), as was consistently noted on the cardioscope. The external pacemaker functioned as a stimulator of intrinsic mechanisms rather than as a substitute for spontaneous ventricular activity.

Therapeutic effects of isoproterenol consisted in stimulation of impulse formations in supraventricular and ventricular centers as well as in improvement of conductivity of the atrioventricular junction (fig. 2, 5-12). This twofold action of the drug has been pointed out previously by us [7] as well as by others.[8] Toxic effects, on the other hand, caused by too rapid infusion consisted in undue acceleration of ventricular impulse formation culminating in almost fatal attacks of ventricular paroxysmal tachycardia which required procainamide medication. Whether or not the paroxysms of auricular fibrillation are to be ascribed to the isoproterenol medication is unanswered. Of considerable theoretical interest is the abrupt termination of auricular fibrillation on one occasion (May 15) by external electric stimulation.

The initial recommended concentration of isoproterenol for intravenous infusion (4 mcg. per cubic centimeter) [2] was found to provide too small a margin between therapeutic and toxic levels. This has also been our experience in other cases of patients with Stokes-Adams disease treated by isoproterenol in this hospital. More dilute solutions, for instance 3 mcg. per cubic centimeters, proved easier to handle and seemed to enhance the safety margin, although it still was difficult to regulate the dose of the medication. Nevertheless, the rapid disappearance of the effects of the diluted drug seems to reduce the dangers of this mode of administration provided constant observation is maintained. The latter is greatly aided by the continuous use of a cardioscope, which was an integral part of the procedure used in this case.

Summary and Conclusions

Survival of a patient with recent posterior wall infarction complicated by frequent attacks of ventricular asystole, as a consequence of a progressively advancing atrioventricular block, is attributed to the prompt and systematic use of an intravenous infusion of isoproterenol in combination with an automatic external pacemaker.

Success or failure of treatment of such cases largely depends on early recognition of impending syncope, on adequate preparations for handling of such an event, and on continuous monitoring of therapeutic measures by a cardioscope. The earliest clinical sign of impending asystole may be the development of a bigeminal pulse.

Recent myocardial infarction complicated by asystole may require the simultaneous use of two sympathomimetic agents: arterenol to maintain the blood pressure and isoproterenol to insure an adequate rate of ventricular contraction. Isoproterenol given as an intravenous infusion is not a harmless drug, and its overdosage may lead to dangerous, rapid ectopic rhythms of ventricular origin. The proper dose may vary from case to case and from moment to moment and requires adjustments under close and continuous observation on a cardioscope.

2011 E. 75th St., (49) (Dr. Solarz).

The external cardiac pacemaker unit used in this study was Electrodyne model PM65, manufactured by the Electrodyne Co., Norwood, Mass.

This study was supported in part by the Hibse Heart Fund for Cardiovascular Research and the Michael Reese Research Foundation.

References

1. Zoll, P. M.: Resuscitation of Heart in Ventricular Standstill by External Electric Stimulation, New England J. Med. **247**:768-771 (Nov. 13) 1952.

2. Zoll, P. M., and others: Intravenous Drug Therapy of Stokes-Adams Disease: Effects of Sympathomimetic Amines on Ventricular Rhythmicity and Atrioventricular Conduction, Circulation **17**:325-339 (March) 1958.

3. Katz, L. N., and Pick, A.: Clinical Electrocardiography, Part I: Arrhythmias, with Atlas of Electrocardiograms, Philadelphia, Lea & Febiger, 1956.

4. Langendorf, R., and Pick, A.: Supernormal Phase of Atrioventricular Conduction, abstracted, Proceedings of Third World Congress of Cardiology, Brussels, 1958, p. 343.

5. Cohen, D. B.; Doctor, L.; and Pick, A.: Significance of Atrioventricular Block Complicating Acute Myocardial Infarction, Am. Heart J. **55**:215-219 (Feb.) 1958.

6. Phelps, M. D., Jr., and Lindsay, J. D., Jr.: Cortisone in Stokes-Adams Disease Secondary to Myocardial Infarction: Report of Case, New England J. Med. **256**:204-208 (Jan. 31) 1957.

7. Pick, A., and Lichtman, A.: Effects of Isuprel in Advanced A-V Block, abstracted, Circulation **16**:925-926 (Nov.) 1957.

8. Schaub, F.; Holzmann, M.; and Wyss, S.: Zur Behandlung von Adams-Stokesschen Anfällen und Überleitungsstörungen des Herzens mit Isopropylnoradrenalin, Schweiz. Med. Wchnschr. **87**:938-946 (July) 1957.

CHLOROTHIAZIDE (DIURIL) AS A HYPERURICACIDEMIC AGENT

Benjamin G. Oren, M.D., Maurice Rich, M.D.
and
Martin S. Belle, M.D., Miami, Fla.

Chlorothiazide (Diuril) has been recently introduced into therapeutics, first, as an effective nonmercurial diuretic [1] and, more recently, as a potentiating hypotensive agent in the treatment of essential hypertension.[2] It apparently has proved to be quite effective in these actions but has a tendency to cause excessive excretion of sodium, potassium, and chloride.[3]

Recently, we noted that in some patients unexplained joint pains could occur, especially in the feet, during the use of this drug. Investigations show no organic cause for this symptom, but the uric acid levels in the blood were found to be elevated. Further investigation of a number of patients receiving this drug confirmed this observation, though joint and foot pain was by no means a uniform symptom. Indeed, some of the highest uric acid levels were associated with no joint pain whatever.

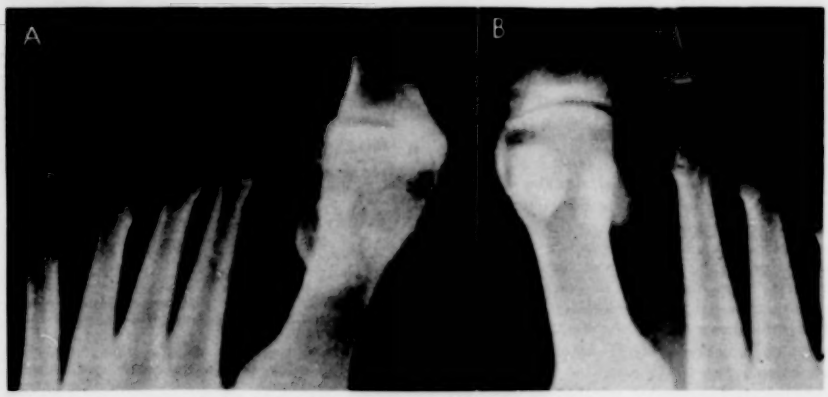
Two significant cases are reported below.

Report of Cases

CASE 1.—A 44-year-old man had been under treatment for essential hypertension for three years, at first with Rauwolfia, subsequently with reserpine (Serpasil). He had suffered a coronary thrombosis two and one-half years ago. It was necessary for him to take 3 mg. of reserpine or its equivalent in order to attain an adequate normotensive effect. However, this large amount of drug resulted in considerable depression and an annoying sluggishness which made it difficult for the patient to continue with his therapy. Accordingly, one year ago associated therapy with chlorothiazide was begun, with smaller doses of reserpine. He was given 500 mg. of chlorothiazide twice daily with 0.25 mg. of reserpine twice daily. This resulted in an adequate control of blood pressure and a return of his mood to normal.

Within three months after institution of this therapy, the patient began to note unusual fatigue and especially pain in the feet on walking and at rest. This was a generalized aching discomfort in both feet. Various attempts to relieve the pain were instituted, including contrast baths, strapping, and various types of shoes, all without much benefit. X-rays showed no evidence of arthritis, tophi, or other organic bone or joint disease. The blood uric acid level was 6.8 mg. % (normal 3 to 5 mg. %). A few days thereafter the chlorothiazide therapy was discontinued, and another uric acid determination 10 days after cessation of the therapy was 4.1 mg. %. The foot pains had disappeared a few days after the discontinuation of chlorothiazide therapy.

Because of the need to control the hypertension, chlorothiazide therapy was again started on Feb. 1, 1958. Within two weeks the aching in the feet had recurred. A blood uric acid determination on June 2, 1958, was 6.6 mg. %. On June 5, chlorothiazide therapy was discontinued. Another determination of uric acid level was made on June 13, at which time it had returned to the normal value of 4.3 mg. %. Again the foot pains had disappeared.



Roentgenograms of both feet in case 2. Note, *A*, destruction of metatarsophalangeal joint space in right foot.

Clinical Associate Professor of Medicine (Dr. Oren) and Clinical Assistant Professor of Medicine (Drs. Rich and Belle), University of Miami School of Medicine.

Case 2.—A 46-year-old man was seen on May 6, 1954, with a history of unexplained hematemesis and melena requiring transfusions in 1950 and another episode of milder hematemesis in April, 1954. He seemed to be in good general physical condition. His blood pressure was 160/110 mm. Hg, and he was somewhat overweight. Gastrointestinal studies showed a minimal deformity of the duodenal bulb, and it was felt that previous episodes of hemorrhage had been from duodenal ulcer. The patient's blood pressure dropped to 110/90 mm. Hg on treatment with Rauwolfia. He got along well on medical therapy, but his blood pressure rose to 170/115 mm. Hg as he discontinued use of medicaments.

On Jan. 16, 1958, he was started on chlorothiazide therapy, 500 mg. twice daily, and reserpine, 0.25 mg. twice daily. The blood pressure thereupon promptly returned to 130/80 mm. Hg, and his weight dropped during the next six months from 197.5 to 168 lb. (89.6 to 75.3 kg.). He felt unusually well except that he began to note increasing pain in the right great toe with prominence at the base of the distal phalanx of the right metatarsal. When seen on Sept. 11, 1958, this had the appearance of gout; the joint was tender and swollen but not hot. On questioning, the patient recalled that he had been told several years previously that he had slight arthritis in the right great toe with small "punched-out areas" appearing on x-ray. Roentgenograms were taken showing destruction of the base of the metatarsophalangeal joint of the right great toe with osteophyte formation (see figure). It was felt that these changes were the result of gouty arthritis. The blood uric acid level was 6.5 mg. %. Chlorothiazide therapy was discontinued, and 12 days later the uric acid level had dropped to 5.4 mg. The pain, swelling, and tenderness in the joint had disappeared, and the patient was asymptomatic. The blood pressure remained at 120/80 mm. Hg.

Comment

The use of chlorothiazide is becoming increasingly prevalent as its hypotensive potentiating effect becomes more clearly established. It seems that in addition to its effect in depleting sodium and potassium levels, this drug has still as yet an unexplained apparent effect on the kidneys, causing them to retain uric acid. Of course, another possible explanation might be an increased catabolism of nucleic acids induced by the drug, but this does not seem likely. Further investigations will probably determine the exact mechanism of action.

This side-effect has hitherto been alluded to only once, by Laragh and his associates.[3a] They noted a significant elevation of serum uric acid level in six of eight patients studied, varying from 7.6 mg. % to 11.5 mg. %. The effect could not be attributed to dehydration, since the blood urea level was not concurrently elevated. In all instances of hyperuricacidemia the patient was asymptomatic and the uric acid level returned promptly to normal values on cessation of therapy.

Our observation confirms those of Laragh and others,[3a] but the uric acid level seems to be even more consistently elevated in patients taking chlorothiazide for any length of time. All 12 patients studied in our group revealed significant elevation of blood uric acid levels, ranging from 6.3 to 10 mg. %. Only three of these patients had joint pains in the feet, and only one (case 2) had positive x-ray findings.

We cannot be sure that true gout is actually caused by this elevation of uric acid level, but it appears that gout-like symptoms can be produced in certain individuals and that the intensity of this effect is not necessarily in direct ratio to the height of the uric acid level in the blood. It is not unlikely that those patients who develop joint pain are potentially gouty individuals in whom symptoms have merely been precipitated. Certainly so valuable an agent as chlorothiazide should not be discarded because of this or other side-effects described thus far. The purpose of this preliminary communication is merely to call attention again to the prevalence of hyperuricacidemia with its use and also to indicate that gout-like symptoms may occur in certain patients. Therefore, we feel that those patients who have a history of gout should be watched with especial care. Further study may clarify the mechanism of this side-effect.

1431 N. Bayshore Dr. (36) (Dr. Oren).

References

1. Ford, R. V.; Moyer, J. H.; and Spurr, C. L.: Clinical and Laboratory Observations on Chlorothiazide (Diuril): Orally Effective Nonmercurial Diuretic Agent, A. M. A. Arch. Int. Med. **100**:582-596 (Oct.) 1957. Becker, M. C.; Simon, F.; and Bernstein, A.: Clinical Evaluation of Chlorothiazide as Diuretic Agent in Congestive Heart Failure, J. Newark Beth Israel Hosp. **9**:58-67 (Jan.) 1958. Pfeiffer, P. H.: Chlorothiazide, Nonmercurial Diuretic Agent, J. Maine M. A. **49**:53-56 (Feb.) 1958.

2. Freis, E. D.; Wanko, A.; Wilson, I. M.; and Parrish, A. E.: Treatment of Essential Hypertension with Chlorothiazide (Diuril): Its Use Alone and Combined with Other Antihypertensive Agents, J. A. M. A. **166**:137-140 (Jan. 11) 1958. Freis, E. D., and Wilson, I. M.: Potentiating Effect of Chlorothiazide (Diuril) in Combination with Antihypertensive Agents: Preliminary Report, M. Ann. District of Columbia **26**:468; 516 (Sept.) 1957. Hollander, W., and Wilkins, R. W.: Chlorothiazide: New Type of Drug for Treatment of Arterial Hypertension, Boston M. Quart. **8**:69-74 (Sept.) 1957. Wilkins, R. W.: New Drugs for Hypertension, with Special Reference to Chlorothiazide, New England J. Med. **257**:1026-1030 (Nov. 21) 1957. Heider, C.; Dennis, E.; and Moyer, J. H.: Chlorothiazide Potentiation of Ganglionic Blockade in Patients with Hypertension, Ann. New York Acad. Sc. **71**:456-464 (Feb. 3) 1958.

3. (*a*) Laragh, J. H.; Heinemann, H. O.; and Demartini, F. E.: Effect of Chlorothiazide on Electrolyte Transport in Man: Its Use in Treatment of Edema of Congestive Heart Failure, Nephrosis, and Cirrhosis, J. A. M. A. **166**:145-152 (Jan. 11) 1958. (*b*) Beyer, K. H.; Baer, J. E.; Russo, H. F.; and Haimbach, A. S.: Chlorothiazide (6-chloro-7-sulfamyl-1, 2, 4-benzothiadiazine-1, 1-dioxide): Enhancement of Sodium Chloride Excretion, Fed. Proc. **16**:282 (March) 1957. (*c*) Ford, R. V., and Spurr, C. L.: Electrolyte Excretion Patterns due to Chlorothiazide, New Orally Effective Diuretic Agent, abstracted, Am. J. Med. **22**:965 (June) 1957.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations. H. D. KAUTZ, M.D., *Secretary.*

CURRENT STATUS OF THE TREATMENT OF ADRENAL DISORDERS

George W. Thorn, M.D., Don H. Nelson, M.D.
and
Albert E. Renold, M.D., Boston

The availability of precise diagnostic techniques and the synthesis of several important adrenal cortical steroids provide the practicing physician with an unusual opportunity for establishing a correct diagnosis and initiating appropriate therapy in patients with abnormalities of adrenal cortical function. The ever-widening horizon of the nonspecific use of adrenal steroid therapy and the exploration of the beneficial effect of hypophysectomy and adrenalectomy have increased greatly the numbers of patients with evidence of altered adrenal cortical function. The development of accurate and clinically applicable measurements of catechol amine levels in blood and urine has enhanced the accuracy with which pheochromocytoma may be detected and has provided a new and important screening technique which should be applied to all patients with hypertension of undetermined origin.

Hormone Preparations

The structural formulas of the adrenal steroid compounds are represented in figure 1.

Corticotropin.—Corticotropin (Acth, Lyophilized Acthar, Corticotropin, Lyophilized Corticotropin), also known as ACTH, adrenocorticotrophin, and corticotrophin, is available as a lyophilized powder, containing 10 to 40 U.S.P. units per vial for intravenous infusion or for intramuscular injection when dissolved in saline solution. Corticotropin is also available as a solution in gelatin, containing 20 to 100 "clinical units" per cubic centimeter, or in combination with zinc as corticotropin-zinc hydroxide (Cortrophin-Zinc) for intramuscular administration only. These preparations provide prolonged activity (18 to 36 hours) after a single intramuscular injection. "Clinical units" are equivalent approximately to one-third U. S. P. units. A U. S. P. unit equals 1 I. U., which, in turn, represents the biological activity of 1 mg. of corticotropin International Standard, as determined by measurement of the adrenal ascorbic secretion in the hypophysectomized rat.

In diseases of adrenal origin the use of corticotropin is confined largely to diagnostic procedures and for stimulating the adrenal cortex after prolonged steroid therapy. The administration of corticotropin, given intramuscularly and particularly intravenously, may precipitate a crisis in a patient with adrenal cortical unresponsiveness unless the patient is protected by the simultaneous administration of a cortisone-like steroid.

Cortisone-like Steroids.—The cortisone-like steroids, also known as 17-hydroxysteroids, are listed as follows.

Hydrocortisone (Cortef, Cortisol, Cortril, Hycortole, Hydrocortone): Hydrocortisone is available in solution in 50% ethyl alcohol, 100 mg. per 20 cc., and as hydrocortisone sodium succinate (Solu-Cortex), 134 mg. of this compound being equivalent to 100 mg. of hydrocortisone for intravenous or intramuscular injection. It is also available as the acetate in saline suspension for intramuscular use (25 mg. per cubic centimeter) and as 20-mg. tablets for oral use. Hydrocortisone, especially the succinate ester, is the only preparation available for immediate and rapid intravenous use. Conversely, the absorption of hydrocortisone acetate after intramuscular injection is much slower than cortisone and hence should be used only when a prolonged effect from a single injection is desired.

Cortisone (Cortisone, Cortogen, Cortone): Cortisone is available as the acetate in saline suspension (25 and 50 mg. per cubic centimeter) for intramuscular use and in tablets for oral use (5, 10, and 25 mg.). For all practical purposes cortisone and hydrocortisone are equivalent milligram for milligram.

From the departments of medicine, Harvard Medical School and the Peter Bent Brigham Hospital (Drs. Thorn, Renold, and Nelson) and investigator, Howard Hughes Medical Institute (Dr. Nelson).

Prednisone (Deltasone, Deltra, Meticorten) and prednisolone (Delta Cortef, Hydeltra, Meticortelone): Prednisone and prednisolone are available as 2.5-mg. and 5-mg. tablets for oral use. One milligram of prednisone or prednisolone is equivalent to 4 to 5 mg. of cortisone or hydrocortisone. Prednisone and prednisolone exert much less sodium-retaining effect, milligram for milligram, than does cortisone or hydrocortisone.

Triamcinolone (Aristocort, Kenacort): Triamcinolone is available as 4-mg. tablets for oral use. One milligram of triamcinolone is equal to approximately 6 mg. of cortisone or hydrocortisone. This substance, milligram for milligram, possesses even less sodium-retaining effect than does prednisone or prednisolone.

Fludrocortisone (Alflorone, F-Cortef, Florinef): Fludrocortisone is available as the acetate in 0.1-mg. and 1.0-mg. tablets. This derivative of hydrocortisone is approximately 25 times as active as cortisone, hydrocortisone, and desoxycorticosterone (Cortate, Decortin, Decosterone, Doca, Percorten); hence, its sodium-retaining action is very great in relation to its cortisone-like action.

Sodium-Retaining Adrenal Steroids.—All adrenal steroids are "sodium-retaining" to some extent under normal conditions. However, unless very large doses of cortisone, hydrocortisone, and prednisone are employed, this activity is not prominent.

Fludrocortisone: Fludrocortisone, as noted previously, is an extremely active sodium-retaining hormone, 1 mg. by mouth being equivalent to 25 mg. of desoxycorticosterone given by injection.

Desoxycorticosterone: Desoxycorticosterone is available for intramuscular injection as the acetate in sesame oil (5 mg. per cubic centimeter). For prolonged effect (15 to 30 days), it is available as a suspension of the trimethylacetate ester (25 mg. per cubic centimeter) and as the acetate in 2-mg. and 5-mg. buccal tablets for sublingual use.

Aldosterone: Aldosterone, the naturally occurring sodium-retaining hormone in man, is not available commercially.

Special Considerations.—The high potency of fludrocortisone, in respect to both its cortisone-like effect and its sodium-retaining effect, makes the administration of this substance particularly advantageous when adrenocorticotropin tests are being carried out. Patients with suspected Addison's disease can be given 1 to 2 mg. of this substance daily while the tests are being conducted, without concern for the hormone derived from this substance which may appear in the urine, since the quantity is so small. Furthermore, larger doses of this substance may be substituted in patients on prolonged cortisone therapy in whom it is desirable to test reserve adrenal capacity before hormone therapy is reduced or discontinued. Thus, 4 to 5 mg. of fludrocortisone is equivalent to 100 mg. of cortisone or hydrocortisone. However, the dietary sodium should be rigidly restricted during the period of substitution to avoid excessive sodium retention. Supplementary potassium chloride (3 to 6 Gm. daily) may also be given.

Acute Adrenal Crisis

Such an emergency may be precipitated in a patient with chronic adrenal cortical insufficiency by the superimposition of stress, such as intercurrent infection, surgery, or trauma. It may also be precipitated in patients on long-term, large-dosage cortisone therapy by the sudden withdrawal of hormone therapy or by the superimposition of stress without an accompanying increase in steroid therapy. Acute adrenal crisis may occur as a complication of anticoagulant therapy (hemorrhage into the adrenal gland) or may present itself as shock in conjunction with surgery, hemorrhage, or acute infection. It is nearly always impossible to establish with certainty the diagnosis of acute adrenal crisis at the time a patient presents the picture of acute hypotensive shock.

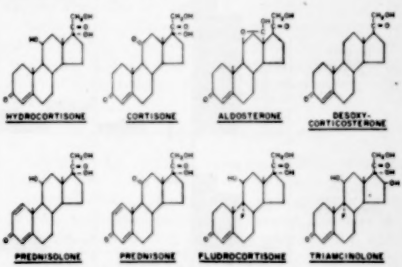


Fig. 1.—Steroid hormone preparations.

Blood is drawn, if possible, for serum steroid determination, and 100 mg. of hydrocortisone sodium succinate, given intravenously, is administered immediately. This procedure may be lifesaving. Pressor amines should be used in conjunction with hydrocortisone in an effort to maintain blood pressure. The use of whole blood, plasma, or albumin and electrolyte solutions given intravenously will be dictated by the circumstances surrounding the circulatory collapse.

If the diagnosis appears to be confirmed by the initial response of the patient to therapy, by the blood steroid values, or by history, then an intravenous drip containing 1,000 cc. of 5% dextrose in isotonic sodium chloride solution, to which is added another 100 mg. of hydrocortisone sodium succinate, is continued, and 100 mg. of cortisone acetate is injected intramuscularly. With the termination of the intravenous infusion, the patient is given 50 mg. of cortisone acetate intramuscularly or orally every 8 hours for the subsequent 24 hours,

then every 12 hours for the next 24 hours, and then a total of 50 to 75 mg. per day by mouth in two or three divided doses or intramuscularly by injection. During this period, in conjunction with the large doses of hydrocortisone and cortisone plus isotonic sodium chloride solution given intramuscularly, no salt-retaining hormone is necessary. When the dose of cortisone is reduced below 75 mg. daily, the use of supplementary saline solution or a salt-retaining hormone, either desoxycorticosterone acetate intramuscularly or fludrocortisone orally, may be required.

Chronic Primary Adrenal Cortical Insufficiency, Including Addison's Disease

A definitive diagnosis of adrenal cortical insufficiency should not be made until a lack of response to intravenously administered corticotropin has been demonstrated, since in the presence of certain abnormal states, such as sarcoid and rheumatoid arthritis, intramuscularly administered corticotropin may not reach the adrenal cortex in adequate concentration. One may follow the urinary steroids or the blood steroid values. The authors prefer the former as being, in general, a more reliable measure of adrenal cortical reserve. The response to corticotropin is also useful in differentiating primary adrenal insufficiency from that secondary to pituitary failure (fig. 2). Blood corticotropin values will be elevated in untreated patients with primary adrenal cortical insufficiency and low or absent in those with pituitary insufficiency.

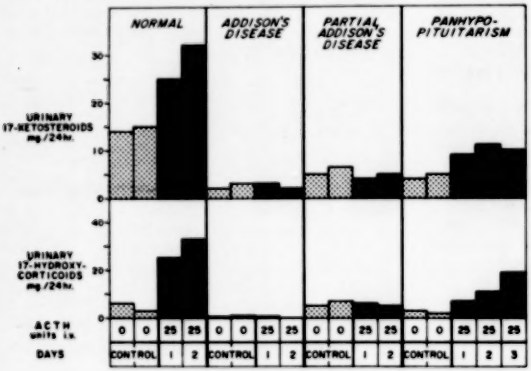


Fig. 2.—Response to intravenously given corticotropin in adrenal insufficiency.

Hormone therapy is indicated in any patient with impaired adrenal cortical reserve who exhibits weakness, weight loss, gastrointestinal symptoms, hyperpigmentation, fasting hypoglycemia, hypotension, abnormal electroencephalographic tracing, or in whom an abnormal response to a water load may be demonstrated. All patients with chronic adrenal deficiency will exhibit improved biochemical and physiological response to stress when given cortisone or one of its derivatives. Whether supplementary sodium chloride or a salt-retaining hormone is required in addition, and how much, will be determined by the patient's blood pressure, cardiac status, serum sodium and potassium levels, hematocrit value, and changes in body weight. The authors prefer to use a small dose of salt-retaining hormone in most patients with Addison's disease unless increasing age, with a rise in blood pressure, or renal and cardiac changes contraindicate.

Cortisone or hydrocortisone by mouth provides the basic maintenance therapy in a dosage of 25 to 50 mg. daily. For most patients one-half to two-thirds of the daily dose is given on arising, the remainder late in the afternoon. Supplementary hormone (50 to 100 mg. daily) is given in the presence of infection or unusual stress. If nausea or vomiting occurs, cortisone may be given intramuscularly; in an acute crisis, the intravenous administration of hydrocortisone is mandatory, as outlined in the foregoing section. The presence of healed or active tuberculosis is no contraindication to cortisone therapy, although the authors limit the maintenance dose to 20 to 25 mg. per day in conjunction with chemotherapy. Under the circumstances, the usual maintenance dose is well tolerated and may even accelerate recovery of the patient.

Adequate cortisone therapy should induce a regression of pigmentation and a gain in weight; hypoglycemic manifestations should be controlled; and a normal diuresis after a water load should be evident. Abnormalities in the electrocardiogram and electroencephalogram should disappear. Initially, chronically deficient patients may exhibit euphoria and an undesirable psychological response to cortisone, so that a dose not exceeding 12.5 mg. per day may be all a patient can comfortably tolerate. Later the dose may be increased slowly to 25 mg., without untoward symptoms. Patients with preexisting peptic ulcer may experience difficulty in tolerating 25 mg. daily of cortisone or its equivalent. In the rare combination of diabetes mellitus and adrenal cortical insufficiency, it is preferable to use a normal maintenance dose of cortisone (25 to 37.5 mg. daily) and sufficient insulin to maintain normal glucose levels. It is desirable for these patients to take part of their cortisone late at night or very early in the morning.

Most patients with chronic adrenal cortical insufficiency will be on maintenance therapy with cortisone or hydrocortisone. There is no advantage

in using a preparation which is less salt-retaining, i. e., prednisone or triamcinolone. In fact, for a few patients, cortisone or hydrocortisone alone with a generous dietary sodium intake may avoid the necessity of supplementary sodium-retaining hormone.

Most patients will do better on a small dose of sodium-retaining hormone. For this purpose, one has three choices: (1) fludrocortisone acetate by mouth in a single daily dose of 0.1 to 0.2 mg.; (2) desoxycorticosterone acetate in oil, the daily intramuscular dose being 1 to 5 mg.; or (3) desoxycorticosterone trimethylacetate, a monthly intramuscular injection of 25 to 75 mg. At a dose level of 0.1 to 0.2 mg. daily, the cortisone equivalent of fludrocortisone can be disregarded, i. e., it will not amount to more than 5 mg. of cortisone equivalent or hydrocortisone equivalent. If larger quantities of fludrocortisone are required, i. e., 0.5 mg. or more, then the cortisone equivalent of this sodium-retaining compound must be considered.

The majority of the authors' patients are on maintenance therapy with either 0.1 to 0.2 mg. of fludrocortisone administered orally daily or 25 to 50 mg. of the long-acting desoxycorticosterone ester given intramuscularly every two to four weeks. Because of the ease with which the oral administration of fludrocortisone can be manipulated, there is a growing tendency to substitute this therapeutic regimen for the monthly injections of long-acting desoxycorticosterone derivatives. Desoxycorticosterone acetate, with a duration of action of 12 to 24 hours, is a useful preparation for a patient who is experiencing nausea, vomiting, or diarrhea in which maximum sodium retention is desirable and in which oral medication may not be well tolerated. A dose of 5 to 10 mg. daily (1 to 2 cc.) of the oil solution given intramuscularly will ensure adequate sodium retention in the presence of normal kidney function. In all instances, it is desirable to establish the optimum dose of sodium-retaining hormone by carefully following changes in body weight, blood pressure, heart size, and serum sodium and potassium levels.

In summarizing, the condition of the majority of patients with primary chronic adrenal cortical insufficiency will be well maintained on a program which includes 25 to 50 mg. daily of cortisone or hydrocortisone and 0.1 to 0.2 mg. of fludrocortisone by mouth. In the presence of complications, the dose of cortisone should be increased immediately.

Chronic Secondary Adrenal Cortical Insufficiency (Hypopituitarism)

In the presence of anterior pituitary deficiency, adrenal cortical insufficiency is modified in three essential respects. First, pigmentation is unusual, due presumably to the fact that corticotropin and melanocyte-stimulating hormone are not present in increased quantities. Secondly, the manifestations of adrenal cortical insufficiency may be tempered significantly by concomitant thyroid and gonadal deficiencies. And thirdly, since corticotropin does not exert the same primary control over aldosterone secretion as it does in the case of the adrenal 17-hydroxysteroids, sodium deficiency may be less pronounced or nonexistent, a fact consistent with relatively normal urinary aldosterone values in patients with pituitary insufficiency. For practical purposes, one treats adrenal, thyroid, and gonadal deficiencies simultaneously in chronic anterior pituitary deficiency. One could employ corticotropin in these patients, but the practical disadvantages of a daily intramuscular injection of hormone favor the use of cortisone or hydrocortisone given orally. The doses of thyroid and cortisone are advantageously increased or decreased simultaneously, as the patient's cortisone requirement may increase with an increased dose of thyroid. Sodium liothyronine (Cytomel), also known as sodium L-triiodothyronine, may have an advantage over thyroid extract or thyroxin in some patients. The dose of cortisone or hydrocortisone in patients with chronic pituitary insufficiency is generally somewhat less than that for patients with Addison's disease. However, in the presence of unusual stress, a large supplement of cortisone will be required.

Iatrogenic Adrenal Insufficiency

Patients who receive prolonged steroid therapy for diseases such as rheumatoid arthritis, disseminated lupus, pemphigus, and asthma may develop temporary or even permanent adrenal cortical inhibition. Presumably the action of the steroids is to depress the hypothalamic-pituitary system. Withdrawal of hormone therapy may precipitate a relapse of the underlying disease, or, if adrenal function is severely inhibited, it may precipitate an acute adrenal crisis. One of the problems encountered in reducing or terminating steroid therapy in such patients is the difficulty of measuring reserve adrenal cortical function without discontinuing therapy.

Today, with the availability of such highly active steroids as fludrocortisone, it is possible to substitute this compound for cortisone or prednisone (i. e., 1 mg. of fludrocortisone for 25 mg. of cortisone or 5 mg. of prednisone) and carry out an adrenocorticotropin test, using the urinary steroid response (17-hydroxysteroids and 17-ketosteroids) as the measure of responsiveness. In this test, corticotropin should be given intravenously (25 units over an eight-hour period is suggested) for at least three days. The small quantity of metabolites of fludrocortisone will not affect the significance of the urinary values. However, when fludrocortisone is used, because of its intense sodium-retaining potency, dietary sodium chloride should be rigidly restricted, but 2 to 6 Gm. of potassium chloride

daily may be given. The period of trial should be kept as short as possible, and a mercurial diuretic or chlorothiazide (Diuril) may be given if excessive fluid retention occurs.

Failure to observe an adequate response to intravenously administered corticotropin, although not necessarily indicating permanent adrenal atrophy, certainly suggests that hypoadrenalism will complicate withdrawal of steroid therapy. Unfortunately, an adequate response to corticotropin does not necessarily indicate that the patient's own hypothalamic-pituitary system will secrete an adequate quantity of corticotropin when steroid therapy is discontinued. At present, there is no practical way of deciding this point without careful withdrawal of steroid therapy and an analysis of baseline urinary steroid values.

This discussion naturally raises the problem of whether one should employ corticotropin therapy, intermittently throughout the course of prolonged steroid therapy, in order to prevent or minimize severe adrenal atrophy. It is true that the adrenal responsiveness may be maintained by such a technique, but unfortunately such a procedure will in no way minimize the hypothalamic or pituitary inhibition which may be the more serious problem. Recent studies have indicated that in disease states, such as asthma, adrenal cortical inhibition may be significantly modified by alternating a high dose of steroids for one to two days with a respite of one to two days, without loss of clinical regulation. This technique has not been applied systematically, nor has the adrenal response been studied accurately in other disease states. However, the program deserves further investigation.

Cushing's Syndrome

The clinical manifestations of Cushing's disease (pituitary basophilism) and those of Cushing's syndrome (adrenal cortical hyperfunction) are due to the production of an increased amount of adrenal steroids. The object of treatment is to decrease or eliminate the abnormal hormone secretion. This can be accomplished with certainty by complete removal of a tumor or of both adrenals if hyperplasia is present, theoretically by chemical inhibition of the pituitary-adrenal secretions or the blocking of the end-organ responsiveness to these hormones, and by ablation (surgery or radiation) of the pituitary when it is the primary site of the disorder.

Cushing's syndrome should be considered in every patient presenting hypertension, diabetes, osteoporosis, or skin manifestations characterized by ecchymoses and striae. Psychological manifestations are also a prominent aspect of the disorder. Definitive diagnosis rests upon detecting a tumor of the pituitary, adrenal, or ovary and the demonstration of an abnormal steroid excretion in the urine. The response to corticotropin and the character of the steroid excretion pattern may prove helpful in suggesting a histological diagnosis, i. e., carcinoma vs. adenoma vs. hyperplasia.

Cushing's syndrome is a serious but usually remediable disorder. It is unfortunate that many patients are permitted to progress to the point that therapy designed to correct the adrenal hormone secretion may not restore the individual to health because of complicating factors such as osteoporosis and fractures, permanent diabetes, hypertension, or severe psychological changes. For this reason, an early and a more radical approach to treatment is to be encouraged.

Tumor of the pituitary is demonstrated rarely. Radiation to the pituitary in such cases should be tried initially unless local pressure signs from the tumor (impairment of vision, headaches) indicate the need for immediate surgical intervention. If irradiation is carried out, there is no need for supplementary hormone therapy; if hypophysectomy is done, the patient should be carried through the operation with substitution therapy, as outlined in the section on acute adrenal crisis. The postoperative care will be that of a pituitary-deficient patient. In the case of removal of a tumor of the adrenal or ovary, the same hormone substitution program is utilized during or after surgery, as outlined in the section on acute adrenal crisis. However, during the immediate postoperative period after removal of a tumor of one adrenal, corticotropin should be tried, with urinary steroid measurements, to determine whether the remaining adrenal cortical tissue will function adequately.

In the presence of bilateral adrenal hyperplasia, the choice lies between an attempt to control the disease by pituitary irradiation, a subtotal adrenalectomy (usually removing one adrenal completely and two-thirds to three-fourths of the second adrenal), or complete bilateral adrenalectomy. The "cures" from irradiation of the pituitary alone are relatively infrequent and unpredictable but can be spectacular. Since several months must elapse before final evaluation of irradiation treatment can be made, it would seem wise to reserve irradiation for those patients in whom the disease is relatively mild and in whom one can be almost certain that tumor exists. As regards the choice of complete or subtotal adrenalectomy, the authors strongly favor the former, since recurrence of the disease is frequent when any adrenal cortical tissue remains and since in practice one must be prepared for adrenal insufficiency, at least in the presence of stress, in the majority of patients with a small remnant of tissue. Experience alone and the seriousness of the disease in the individual patient must weight the judgment of the physician and surgeon in determining the risk of recurrence if any tissue is left and the certainty of adrenal cortical insufficiency if all tissue is removed.

In recent years the development of hyperpigmentation, despite a level of cortisone adequate for all other needs, has been observed in certain adrenalectomized patients. This may occur in association with progressive enlargement of the sella turcica. Whether irradiation of the pituitary, carried out prior to or after adrenalectomy, will prevent or correct this evidence of excessive corticotropin or secretion of the melanocyte-stimulating hormone remains to be seen.

After adrenalectomy in patients with Cushing's syndrome, the dosage of cortisone or hydrocortisone must be followed carefully. Too rapid reduction may result in symptoms of acute adrenal insufficiency in a patient whose tissues have adjusted over the years to a relative excess of hormone. On the other hand, the prolonged administration of excessive doses of cortisone may accentuate the symptoms of Cushing's syndrome. With a good urine output, patients should be given generous quantities of potassium during the immediate postoperative period, i. e., at least 40 to 80 mEq. per 24 hours. In general, the dose of cortisone will be 300 mg. on the day of operation, 200 mg. on the first postoperative day, 150 mg. on the next, then 100 mg. for two to three days, 75 mg. for one week, and, finally, 50 to 62.5 mg. daily for an indefinite period. When the dose of cortisone is reduced below 75 mg. per day in the bilaterally adrenalectomized patient, additional salt or supplementary sodium-retaining hormone will be required, i. e., 1 to 5 mg. of desoxycortieosterone acetate given intramuscularly once daily or 0.1 to 0.2 mg. of fludrocortisone orally. Potassium supplementation, 3 to 6 Gm. daily, if tolerated, and testosterone propionate (25 mg. weekly for female patients) should be continued indefinitely if tolerated.

Adrenal Virilism and the Adrenogenital Syndrome

The clinical manifestations of excessive adrenal androgen secretion may be caused by a tumor or hyperplasia of the adrenal cortex. Steroid analysis of the urine, particularly the 17-ketosteroids, and fractionation of the 17-ketosteroids into those derived from hydrocortisone and those derived from adrenal androgens will be of specific diagnostic aid. Studies on the inhibition of adrenal androgen by cortisone or its derivatives, preferably prednisone or fludrocortisone, will be of additional help in differentiating tumor from hyperplasia and indicating whether medical therapy, i. e., long-continued cortisone therapy, is therapeutically feasible or whether surgery must be resorted to if the disorder is to be cured. The use of the most potent cortisone-like substances in the suppression test is to be encouraged, since the small quantity of ketosteroids derived from the exogenously administered hormone will not interfere significantly with the evaluation of the test. It is helpful to note that prednisone is not excreted as 17-ketosteroid material and hence can be advantageously used. This substance does, of course, give rise to increased 17-hydroxysteroid material in the urine.

Patients with virilism or the adrenogenital syndrome may display evidence of deficiency of sodium-retaining hormone. Under these circumstances, the clinical picture may be complicated by the presence of hypotension, weakness, small heart size, azotemia, hyponatremia, and hyperkalemia. The use of fludrocortisone (0.1 to 0.2 mg. daily by mouth) or a biweekly or monthly injection of the long-acting desoxycorticosterone trimethylacetate given intramuscularly (25 to 50 mg.) should provide satisfactory regulation. The dosage will, of course, be adjusted to maintain a normal blood pressure and electrolyte balance.

If a tumor is suspected in a patient with virilism or adrenogenital syndrome, surgery is advised; the care of the patient is similar to that outlined under Cushing's syndrome, with the exception that the cortisone dosage may be reduced much more rapidly postoperatively since hypercorticism was not present initially. A trial with corticotropin is essential, however, to test the adequacy of the remaining adrenal tissue before supplementary hormone is withdrawn completely. There is usually no need for potassium medication, testosterone, or sodium-retaining adrenal steroid therapy.

The problem is more difficult when virilization or adrenogenital syndrome is due to bilateral adrenal hyperplasia. If adequate suppression can be obtained with a dose of cortisone or cortisone-like steroid which will not induce the undesirable side-effects of Cushing's syndrome, medical management is feasible. Cortisone or hydrocortisone given intramuscularly is recommended for the initiation of treatment, i. e., 100 mg. daily for adults and older children; 25 mg. daily will suffice for infants. The minimum dosage required subsequently will be determined on the basis of the 24-hour urinary ketosteroid excretion. An effort should be made to maintain the level of 17-ketosteroids below 2 mg. in infants, below 7 mg. in older children, and below 10 mg. in adults. Infants will require 25 to 37.5 mg. of cortisone intramuscularly every three or four days; older children will require 50 to 100 mg. every three or four days. The dosage of hormone given orally will be two to three times that employed intramuscularly. The excreted products (17-ketosteroids) from the administered hormone will complicate the interpretation of the suppressive action of the therapy unless substances such as prednisone are used.

It is desirable to use supplementary potassium medication, i. e., 3 to 6 Gm. of potassium chloride daily, in an effort to minimize the hypochloremic, hypokalemic alkalosis which is so characteristically induced by long-term steroid therapy. The return

of normal menstrual periods, the disappearance of acne, the regression of body hair, and the attainment of a normal female configuration comprise the criteria of success. Unfortunately, the inhibition of excessive hair growth may be very difficult to attain with steroid therapy.

In the event that suppression of androgen secretion cannot be obtained with a dose of cortisone-like steroid, which in turn does not induce Cushing's syndrome, one is faced with a difficult decision. Should one proceed with adrenal resection? In contrast to the approach to a patient with Cushing's syndrome, which is in itself life-threatening from a clinical viewpoint, mild virilism or the adrenogenital syndrome is not life-threatening, except in its serious psychological implications. If surgery is undertaken, the following steps are suggested:

1. Unless the adrenals are approached by an abdominal incision which permits the exploration of the ovaries, a pelvic exploratory operation or a culdoscopy with visualization of the ovaries must be undertaken before adrenal surgery. Such an initial step will permit the physician to evaluate ovarian function and the possibility of ovarian disease and to exclude the ovary as a source of androgen-secreting tissue.

2. In contrast to the approach to a patient with Cushing's syndrome in which radical bilateral complete adrenalectomy is to be encouraged, the patient with adrenal hyperplasia and the adrenogenital syndrome would do well to have one adrenal removed and only a portion of the second, in the hope that control of the syndrome might be accomplished by a more conservative procedure. No great difficulty should be encountered if a second, complete adrenalectomy is ultimately deemed necessary. The operative and postoperative needs for hormone therapy will be similar to those noted previously. Again, if a subtotal adrenalectomy is performed, a response to corticotropin should be undertaken prior to discontinuing supplementary hormone therapy. Of course, if sodium-retaining hormone had been required preoperatively, it will be necessary to continue this therapy. In addition, patients with unilateral adrenal removal and partial resection of the second gland may require supplementary sodium chloride or sodium-retaining hormone (fludrocortisone) by mouth once daily, desoxycorticosterone trimethylacetate given intramuscularly once monthly, or desoxycorticosterone acetate in oil, intramuscularly for daily use.

Finally, no patient with menstrual irregularities and a virilizing syndrome should have her adrenal explored (in the absence of a securely documented, unilateral adrenal mass) until ovarian exploration has been carried out. A deficiency of mineralocorticoids should also be excluded in all adrenogenital cases.

Primary Hyperaldosteronism (Conn's Syndrome)

All patients with hypertension, with unexplained episodes of weakness, with unexplained hypochloremic, hypokalemic alkalosis, and with unexplained polyuria and polydipsia should be screened for primary hyperaldosteronism. The majority of patients with primary hyperaldosteronism do not exhibit edema. The latter finding is characteristic of secondary hyperaldosteronism. A definitive diagnosis of primary hyperaldosteronism may be difficult to establish, because urinary aldosterone determinations are difficult to carry out, and normal values have been encountered in well-documented cases. It was hoped that a determination of the salivary sodium:potassium ratio, which can be easily measured, might provide a readily available screen for cases of primary hyperaldosteronism, since aldosterone is known to affect the sodium concentration of saliva. At present it can be stated that a value of more than 0.5 in salivary sodium: potassium ratio is strong evidence against excessive aldosterone secretion at that time. (The test is carried out in the morning, with care being taken that no dentifrice or other sodium-containing medication has been used; the analysis is made on the second 10-minute specimen with paraffin chewing, the first 10-minute specimen having been discarded.) Values of less than 0.5 are frequently found in secondary hyperaldosteronism and probably in other conditions. Whether the salivary sodium:potassium ratio will assist in excluding the many patients who do not need definitive hormone studies remains to be seen. Of course, every patient with unexplained hypertension should have pyelograms, which may prove helpful in detecting a large tumor. Unfortunately, small tumors or bilateral adrenal hyperplasia are not likely to be detected by this means.

The diagnosis of primary hyperaldosteronism should be considered seriously in the presence of hypertension and hyperchloremic, hypokalemic alkalosis with a normal potassium content of the urine, i. e., 40 to 50 mEq. or more per 24 hours. Sodium restriction and potassium medication should ameliorate the symptoms, whereas unrestricted sodium and low-potassium intake should aggravate the disorder. Changes in the electrocardiogram, suggesting hypokalemia, may initiate the search for the disorder in patients with hypertension and cardiac abnormalities.

Since primary hyperaldosteronism is a life-threatening disorder, an active and aggressive attitude should be taken toward the diagnosis and treatment of the syndrome. The removal of a tumor presents no unusual therapeutic problems except that a generous potassium supplement should be provided preoperatively and postoperatively. An aldosterone-secreting tumor will inhibit the production of aldosterone by the opposite adrenal but will

not inhibit the adrenal secretion of 17-hydroxysteroids and androgenic steroids. Postoperatively, one must watch for excessive sodium loss and be prepared for the administration of supplementary sodium salts or salt-retaining hormone as needed. In the absence of a tumor, a complete bilateral adrenalectomy may be necessary in a patient with hypertension and unexplained hypokalemia. Histological examination of the adrenals, certainly frozen sections, may not prove helpful in guiding the surgeon.

The operative and postoperative care of such patients, as far as adrenal hormone replacement is concerned, is identical with that previously described. However, since hypercorticism did not exist preoperatively, one may attain normal cortisone-replacement levels relatively rapidly after operation. Again, hypokalemia is probably the most serious immediate postoperative complication. One note of caution should be mentioned. Since patients with this condition may lose sodium rapidly and in large quantities postoperatively, if unsupervised, the patient may develop hyperkalemia as a consequence of excessive sodium loss and supplementary potassium medication at a time when his body tissues are markedly depleted of potassium. Daily serum sodium and potassium determinations are essential in the immediate postoperative management of these patients.

Secondary Hyperaldosteronism

The syndrome of edema, associated with increased urinary values for aldosterone, implies a causal relationship between secondary hyperaldosteronism and the edematous state. Four points deserve consideration. 1. An increase in urinary aldosterone excretion does not necessarily, but in all probability does, imply increased aldosterone production. 2. It has been shown that patients with heart failure and generalized edema may have normal aldosterone values until treatment is instituted. 3. A decrease in aldosterone excretion has been attained with adrenal inhibition, without a concomitant increase in sodium excretion, suggesting that, in such cases, secondary hyperaldosteronism was not at that particular time the determining factor in the production or maintenance of the edematous state. 4. A decrease in aldosterone excretion produced by inhibition of adrenal secretion or the administration of a competitive substance has resulted in a sodium diuresis in certain patients with edema and elevated urinary aldosterone values. In these patients it is presumed that secondary hyperaldosteronism has been an important factor in the genesis or maintenance of the edematous state. Finally, adrenalectomy in certain patients with edema has been followed by a sodium diuresis and marked clinical improvement in patients with hypertensive cardiovascular disease, the nephrotic syndrome, and cirrhosis with ascites.

From these considerations there is little doubt that secondary hyperaldosteronism is a frequent concomitant of the edematous state. There is considerable uncertainty as to its importance at any given stage in a patient's decompensation. Medical inhibition of aldosterone production or competition with the action of aldosterone on renal tubular mechanisms would appear to be the most promising approach to the clinical problem. Bilateral complete adrenalectomy for secondary hyperaldosteronism should be reserved for those patients in whom a direct relationship between sodium retention and hypersecretion of aldosterone can be demonstrated, and in whom the risk of major surgery may be justified by an important degree of or prolonged clinical benefit. The specific hormone requirements for the management of such patients will be similar to those employed in other cases of bilateral adrenalectomy, with the exception that cortisone-like steroids of less sodium-retaining capacity, i. e., prednisone and triamcinolone, will, in general, be preferred during the postoperative period.

Pheochromocytoma

Recent advances in the chemical determination of catechol amines in the blood and urine have provided definitive techniques for detecting the presence of pheochromocytoma in patients presenting paroxysmal or sustained hypertension, particularly when associated with anxiety, dizziness, palpitation, nausea, vomiting, sweating, precordial pain, and peripheral vasoconstriction.

After the demonstration of a tumor or elevated levels of urinary or blood catechol amines, surgical exploration should be undertaken. The use of intravenously administered phentolamine (Regitine) methanesulfonate prior to and during operation may be lifesaving in preventing an excessive rise of blood pressure. A solution of this substance should be available throughout the operation. Later with the ligation of adrenal vessels and the removal of a tumor, one must be prepared for a sudden and precipitous fall in blood pressure. This may be corrected by the use of levarterenol (Levophed) bitartrate given intravenously (never subcutaneously or intramuscularly). Phenylephrine (Neo-Synephrine) hydrochloride may be given subcutaneously to correct mild hypotensive episodes. Perhaps the most important postoperative maneuver is to keep the patient undisturbed for several hours on the operating-room table, as a sudden change in posture may precipitate collapse. Postoperatively, adrenal steroid therapy is not required unless a bilateral adrenalectomy has been performed. Postoperatively, the blood pressure can be controlled with phenylephrine. In the more severe cases it may require 48 to 72 hours before supportive medication can be withdrawn.

This study was supported, in part, by grants from the Eugene Higgins Trust, Harvard Medical School, and the John A. Hartford Foundation, New York.

COUNCIL ON FOODS AND NUTRITION

The following is one of the six papers presented at the symposium on "Nutrition in Pregnancy" in Columbia, Mo., Oct. 11, 1957. This symposium was sponsored by the Council on Foods and Nutrition, with the cooperation of the Boone County Medical Society, the University of Missouri School of Medicine, and the Adult Education and Extension Service of the University of Missouri.

PHILIP L. WHITE, Sc.D., *Secretary.*
Council on Foods and Nutrition

VANDERBILT COOPERATIVE STUDY OF MATERNAL AND INFANT NUTRITION

XII. EFFECT OF REPRODUCTIVE CYCLE ON NUTRITIONAL STATUS AND REQUIREMENTS

William J. McGanity, M.D., F.R.C.S.(C), Edwin B. Bridgforth, A.B.
and
William J. Darby, M.D., Ph.D., Nashville, Tenn.

Numerous reports concerning the influence of maternal nutrition upon the course of pregnancy or the health of the infant have appeared during the past 20 years. These have led to the concept that the increased physiological nutritional requirements during pregnancy and lactation enhance the likelihood of nutritional deficiencies occurring during the reproductive interlude. Metabolic adjustments during this period may so alter the metabolism in some patients that a conditioned deficiency state may develop in spite of what would otherwise be considered an adequate dietary intake. The expectation of these alterations in nutrient requirement is reflected in estimates of nutrient allowances such as the Recommended Dietary Allowances of the Food and Nutrition Board.[1]

It has been hypothesized that a number of maternal and fetal complications peculiar to the reproductive interlude may be related to the nutritional level of the mother's diet.[2] From studies, such as Warkany's, on a variety of species of experimental animals, it is clear that the maternal nutritional level can influence fetal development, viability, birth weight, and other physiological attributes of the newborn animal. However, extrapolation from laboratory findings to situations commonly encountered in obstetric practice has resulted in inconsistencies and confusion of claims. Some of these have arisen as a result of the physician's failure to distinguish between conditions of obvious nutritional origin and conditions in which the etiology may possibly have a nutritional component.

Prior to any consideration of the effects of reproduction on maternal nutrition, it is desirable to recognize and to identify the present-day expectant mother in America. To base our premise on her pre-World War II status would be a gross injustice. Although obesity remains a national nutritional problem, the young mother of today is no longer willing to accept obesity as her price for having children, and she is doing something about it even prior to conception. Recent reports [3] have indicated that the average caloric consumption by nonpregnant, nonlactating women is 400 to 500 calories below the National Research Council's dietary allowance. This should be anticipated when one compares the modern woman's conservation of energy, resulting from our present-day centrally heated, motorized, and mechanized culture, with the energy expended by women in the past.

The metabolic and physiological changes during the reproductive interlude are manifest in every organ and system of the maternal body. We do not always take cognizance of the fact that the 40 weeks of gestation is the period of the most rapid growth and development known to medicine, that pregnancy is the most potent anabolic force we have, or that there is a placental barrier. It is also necessary to recall that alterations such as increased basal metabolism and blood volume, and decreased gastric acidity, gastrointestinal motility, and renal threshold do occur and may influence significantly one's interpretation of maternal nutriture.

It is the unquestioned aim of maternal nutriture to provide adequate amounts of the essential nutrients from conception through parturition and lactation. These nutrients provide for the mother's maintenance and the growth and development of the fetus and protect each from complications during or after the reproductive cycle.

Dietary, Biochemical, and Clinical Assessment

We have had the opportunity of making nutritional observations on a total obstetric clinic population over a period of years at Vanderbilt. The sample consisted of 2,338 pregnant white women who presented themselves for prenatal care at the

From the Department of Obstetrics and Gynecology and Preventive Medicine and the Division of Nutrition of the Department of Biochemistry, Vanderbilt University School of Medicine.

outpatient clinic. Economically, these patients fell into the lower income brackets ($1,200 to $3,000 per annum). From this study we obtained an objective quantitative description of changes that occur in nutritional physiology during the reproductive interlude. Our results were based on obstetric and pediatric performance and dietary, biochemical, and clinical assessment obtained prior to the recognition or development of any abnormality. The several observations were repeated during each trimester and at the postpartum examination. From the data amassed, the effect of pregnancy and lactation on maternal nutritional status was determined, and a yardstick was provided for nutritional requirements in pregnancy. A great effort was made to prevent revealing the results of the nutritional estimates to the physician or patient. This avoided influencing management of the diet.

TABLE 1.—*Average Daily Nutrient Intakes for Each Trimester*

	Trimester		
	1st	2nd	3rd
Diet records, No.	278	1,222	1,665
	Means		
Total calories	2,140	2,200	2,020
Protein, Gm.	75	75	70
Calcium, Gm.	1.1	1.1	1.0
Iron, mg.	13	14	13
Thiamine, mg.	1.5	1.5	1.4
Niacin, mg.	12	12	11
Riboflavin, mg.	2.5	2.5	2.3
	Medians		
Total vitamin A activity, I.U.	6,500	6,600	5,900
Vitamin C, mg.	66	62	55

Nutrient Intakes.—The average daily nutrient intakes of this group of patients are indicated in table 1. We did not (and do not) routinely prescribe pharmaceutical supplements in our clinic. Seventy-three per cent of our patients received no dietary supplement. In the remaining 27%, the type and period of supplementation varied, but it was seldom extended throughout the whole period of gestation. In calculating nutrient intakes, the contribution made by pharmaceutical supplements is not included. Although these average nutrient intake levels are not all equal to those of the recommended allowances from the Food and Nutrition Board, they are not disturbingly low. There is a somewhat surprising decrease of approximately 200 calories in intake between the second and the third trimester. This is associated with a similar decrease in the consumption of most of the other individual nutrients. As will be seen subsequently, considerable variation occurred around these average figures. The food patterns of these women were gratifyingly varied and revealed no widespread disturbing food prejudices or fads associated with pregnancy. Their diets showed frequent consumption of the necessary basic nutrients supplied by milk and eggs, green and yellow vegetables, and citrus and other fruits. Individuals revealed a remarkable degree of constancy of nutrient intake between successive trimesters and even successive pregnancies.

Why did the decrease in caloric consumption between the second and the third trimester occur? Is it a reflection of maternal design or of the physician's advice? We know that the physician's advice was responsible, in a large part, for the decline in caloric intake of patients who were obese, who gained weight rapidly, or who were preeclamptic. However, the decreased intake was not limited to these categories. It appears that the recommended standards of caloric intake during pregnancy are too high for today's expectant mother. It is reasonable to postulate that the reduced intake during the latter months of pregnancy reflects lessened activity on the part of the mother.

Changes in Body Fluids.—The biochemical measurement of body fluids revealed nutrient levels consistent with values that one expects in healthy populations. In both the blood and the urine several alterations in nutrient levels were found. These reflected gestational lactational influences and revealed significant differences in nutrient concentrations when compared with nonpregnant values. These alterations fell into the following categories: 1. The mean hematological values (but not the indexes), total serum protein, and serum vitamin A, and the urinary excretion of thiamine and riboflavin showed a decline in concentration during the first 32 to 34 weeks of gestation and a postpartum rise, mirroring the changes in circulating blood volume. Figure 1 illustrates this pattern for serum protein determinations. The dietary intake of these nutrients does not account for this observed biochemical change. 2. For the mean levels of serum carotene and tocopherol and the urinary excretion of N'-methylnicotinamide, a progressive increase in concentration during pregnancy and a postpartum decline were found. Figure 2 shows this for serum vitamin A and carotene levels. For the two fat-soluble vitamins, the pattern suggests that the lipid-transporting ability of the serum is increased during

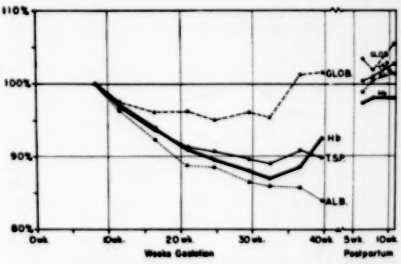


Fig. 1.—Serum protein determinations by weeks of gestation as percentage of 5-to-8-week values.

pregnancy, paralleling the known increase in serum cholesterol value. Again, this alteration was not related to the intake levels of any of the nutrients. 3. The mean serum ascorbic acid concentration decreased slightly during gestation (fig. 3). However, when the dietary intake of vitamin C was above 80

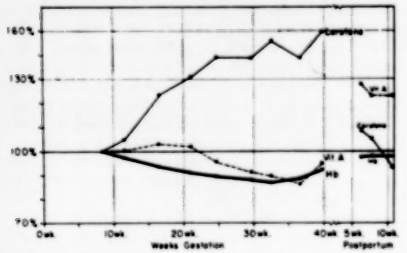


Fig. 2.—Serum vitamin A and carotene determinations by weeks of gestation as percentage of 5-to-8-week values.

mg. per day, this decline during the prenatal phase did not take place. A further sharp decline occurred post partum in the group of women (71%) who breast-fed their infants. Mothers who fed their infants artifically did not exhibit this postpartum drop-off. This evidence of lactational change appeared at all levels of intake of vitamin C.[4] 4. There was a progressive increase in the absorption and utilization of iron as pregnancy advanced (fig. 4). During the last 10 weeks of pregnancy, the uptake of iron was three times that of the first trimester level.[5]

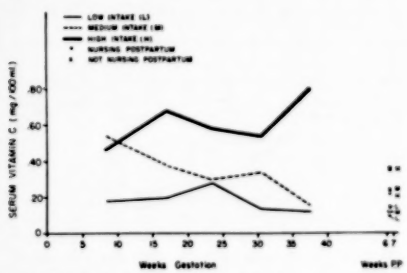


Fig. 3.—Median serum vitamin C levels in consistent intake groups, February to June.

All these alterations reflect metabolic changes of apparently normal physiological origin. To assay biochemical measurements during the reproductive interlude against normal nonpregnant, nonlactating values reveals a lack of understanding of the fundamental adjustments occurring in the pregnant and lactating mother.

Obstetric Complications.—The obstetric and pediatric details of our study have been reported.[6] Suffice it to say that the age and parity relationship of the group reflected a normal pattern. Table 2 dem-

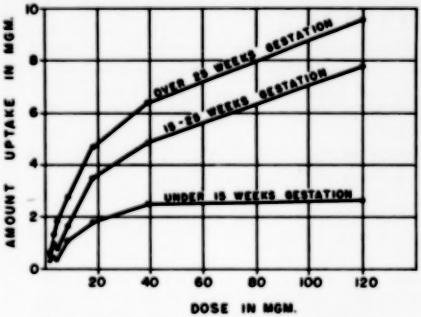


Fig. 4.—Relationship between median amount uptake of iron and dose level during three periods of pregnancy.

onstrates that this population may be considered as an average, or slightly better than average, obstetric population encountered in the United States. This supports the validity of the generalization of our results.

The mean height of the women included in the study was 64 inches. The median weight increased from 122 lb. (55.3 kg.) in the first trimester to 139 lb. (63.0 kg.) in the third trimester and then dropped back to 126 lb. (57.1 kg.) at the time of the examination six weeks post partum. Obesity was

TABLE 2.—*Percentage Incidence of Some Obstetric Complications*

	National Estimates, %*	Vanderbilt Study, %
Anemia	10	11.3
Preeclampsia	6-7	4.5
Eclampsia	0.7	0.5
Placenta previa	0.5-1.0	0.4
Premature separation of placenta	0.3-1.0	1.2
Abortions, spontaneous	10	4.4
Prematurity	6-12	6.7
Twins	1.2	1.1
Breech presentation	3.0	3.9
Cesarean section	2.0	3.2
Postpartum hemorrhage	1-6	1.0
Puerperal morbidity	...	5.4
Congenital malformations	2.5-3.0	2.6
Stillbirths/100 total births†	1.84	1.5
Neonatal deaths/100 total births†	2.12	2.0

* Widely accepted national or textbook figures.
† Average rate in United States for whites, 1946 to 1950.

recorded for 15.7% of the women and varied from 11.5% during the first trimester to 19.3% during the third trimester of pregnancy. Undernutrition was least frequently seen during the last trimester.

As would be expected, the occurrence of dependent edema and varicosities was greater in the latter half of gestation, reaching a peak in the third

trimester and returning to more usual levels post partum. No instances of clinically recognizable deficiency disease were encountered during the reproductive interlude.

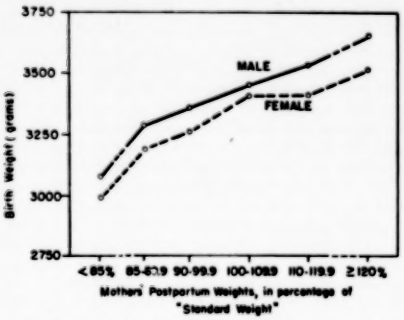


Fig. 5.—Relationship between average birth weight of live-born singletons and mothers' postpartum weights.

Although the average findings revealed a satisfactory status for the group as determined by dietary, biochemical, and clinical assessment and by obstetric and pediatric performance, some women were underweight or overweight, some ate poorly, some ate excessively, some had low blood and urinary levels of nutrients, and some had obstetric and pediatric difficulties. Further examination of these factors may point out weaknesses in maternal nutriture and provide a basis for establishing nutrient requirements during the reproductive interlude.

Weight Status.—The mean height and weight data by trimester revealed an average woman with an acceptable weight gain for her pregnancy. The underweight group (less than 85% standard weight) recorded the highest dietary intakes and was concentrated in the lower parity groups, for as parity went up, the incidence of underweight declined. In this group, there was an increased frequency of mothers who artificially fed their infants and an increased incidence of prematurity. However, the latter should be anticipated because of the linear relationship between the mother's usual percentage of standard weight and the birth weight of the infant (fig. 5). On the other hand, the underweight group had fewer neonatal deaths and congenitally malformed infants.

The overweight group (greater than or equal to 120% of standard weight) increased as age and parity advanced. Among primigravidas who were under 30 years of age, obesity was observed in 15% of the group, whereas among women over 30 years of age and/or para IV or more 36% were overweight. The overweight group had the lowest recorded dietary intakes. There were significantly higher mean hematological and serum protein and vitamin A values, a threefold increase in preeclampsia, more stillborn children, and a lowered frequency of puerperal morbidity.

Regardless of weight status, there were high weight gainers in all groups—underweight, normal, and overweight—and with all ages of women. These high gainers ate more, particularly during the second trimester, and had more toxemia. It is clear from our data that the physician clamped down on the nutrient intake of both the overweight and high weight gainers. In the obese women with high weight gains, the caloric intake was reduced an average of 900 calories from the first to the third trimester.

Low Hemoglobin Group.—Consideration of maternal and fetal iron needs, iron absorption and utilization, and normal gestational alterations in hematological values is necessary prior to discussing the problem of anemia. In a normal pregnancy, the expectant mother will require the absorption and utilization of 700 to 1,000 mg. of elemental iron for her own needs and those of the fetus. If bleeding is absent during gestation, she is able to conserve about 240 mg. of elemental iron as a result of the cessation of the menstrual loss. In addition, her ability to absorb and utilize iron is enhanced at least threefold during the third trimester when her own and the fetal demands are greatest. Coincident with the changes in circulating blood volume (plasma and red blood cell volume) and increased hemoglobin mass, there is a progressive fall in the mean hematological values until the 32nd to 34th week of gestation and then a significant rise prior to delivery that continues upward during the puerperium. In the case of the hemoglobin, this

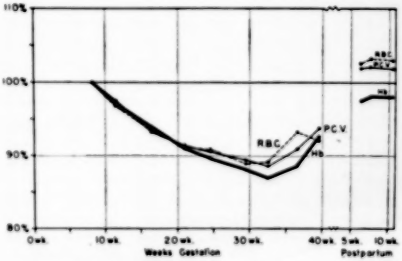


Fig. 6.—Hematological determinations by weeks of gestation as percentage of 5-to-8-week values.

rise amounts to 0.8 Gm. per 100 ml. during the last six to eight weeks of gestation (fig. 6) and is independent of either nutrient iron intake or iron supplementation. An alternative manner of presenting this rise is shown in figure 7. Here the hematological

values at delivery are considered the 100% line (not all women delivered at 40 weeks of gestation). It is apparent that the average hemoglobin value at 18-to-20-week gestation is the same as it will be at

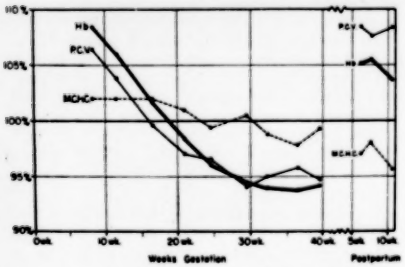


Fig. 7.—Hematological determinations by weeks of gestation as percentage of delivery values.

the time of delivery. These alterations in hematological values were associated with minimal depression of the blood indexes (fig. 8). The decrease in mean cell hemoglobin concentration (MCHC) in the third trimester seems to reflect the increased need for iron by the mother during the latter portion of her pregnancy, a need which was apparent in the pattern of absorption and utilization of this element. The more pronounced decrease apparent in the puerperium is, in all likelihood, the result of blood loss occurring during or after delivery.

The "low hemoglobin group" consisted of women who had a hemoglobin level of less than 10 Gm. per 100 ml. On this basis, 232 (11.3%) were so classified—10.5% during the prenatal phase and 0.8%

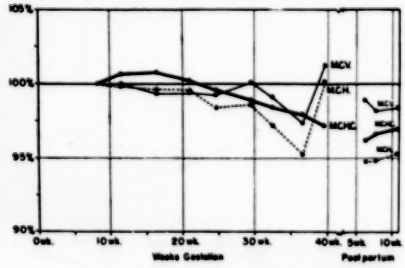


Fig. 8.—Blood indexes by weeks of gestation as percentage of 5-to-8-week values.

in the puerperium. Of the 196 women who had hemoglobin values below 10 Gm. per 100 ml. in the third trimester, not more than 27% had blood indexes indicative of iron deficiency anemia (table 3). In the total study group of 1,974 there were only 4% who had either a mean cell volume (MCV) or a mean cell hemoglobin concentration (MCHC) indicative of iron insufficiency. Two hundred sixteen of the women developed their low hemoglobin values during the prenatal period (148 in the third trimester), 209 of them having hemoglobin levels above 10 Gm. per 100 ml. at the time of their postpartum examination. The remaining 7 women, plus an additional 16, revealed low hemoglobin values (less than 10 Gm. per 100 ml.) at the time of postpartum examination. From the observations indicating excessive blood loss during the latter half of pregnancy, delivery, or puerperium, it is evident that this group had a conditioned iron deficiency.

The iron and vitamin C intakes of the low hemoglobin group tended to be lower throughout the whole of pregnancy when compared with the intakes of these nutrients by the other groups. However, it is difficult to accept mean intakes of 12 mg. of iron and 46 mg. of vitamin C as deficient values. In the group with hemoglobin levels below 10 Gm. per 100 ml., there was a general lowering of the

TABLE 3.—*Distribution of Hemoglobin Values*

	Third Trimester Hemoglobin, Gm./100 Ml.				
	<10.0	10.0-10.9	11.0-11.9	≥12.0	Total
Patients, no.	196	331	569	878	1,974
Patients, %	10	18	29	43	100
Patients with packed cell volume, <30%, %	32	1	0	0	3
Patients with mean cell volume <75 cu. μ, %	19	5	2	1	4
Patients with mean cell hemoglobin concentration <30%, %	27	6	2	0	4
Patients with mean cell volume <75 cu. μ and mean cell hemoglobin concentration <30%, %	9	0	0	0	1

other blood and serum determinations and an increased incidence of dependent edema in keeping with an increased circulating plasma volume.

Only 35% of the low hemoglobin group received prescriptions for supplemental iron, and there were no differences in the recorded dietary intakes of iron between women who were supplemented and those who were not. During the third trimester the MCV and MCHC of the group receiving supplements remained significantly lower than in the group not receiving supplements. It was not until the postpartum examination that these hematological differences between the supplemented and the unsupplemented group disappeared. This was particularly noteworthy for patients who had excessive loss of blood during the prenatal period, at delivery, or during the puerperium due to factors such as placenta previa, premature separation of the placenta, postpartum hemorrhage, and, possibly, abortion. At the time of postpartum examination, those patients with excessive blood loss had hemoglobin levels as much as 1.8 Gm. below the values for the total study group. In spite of what was considered unit-for-unit blood replacement and some supple-

mentation with iron during hospitalization, there was failure to replace the patient's blood loss by approximately 500 ml. This is conditioned iron deficiency. The need for iron supplementation in such instances is evident.

Strauss [7] has demonstrated that the children of mothers who have severe iron deficiency anemia at term are themselves anemic at one year of age. Our data [8] on the mothers with low hemoglobin levels at delivery (fig. 9) reveal no differences in the infants' hemoglobin levels during the first year of life when compared with those of infants delivered of mothers in the high hemoglobin group. Although the mothers in our study did not exhibit a major degree of iron deficiency, it is evident that, even if the infant's iron stores at delivery were inadequate, proper infant feeding during the first year of life was corrective and preventative.

Lactation.—The period of maternal lactation has been less well studied than the gestational phase. The obstetrician, pediatrician, and general practi-

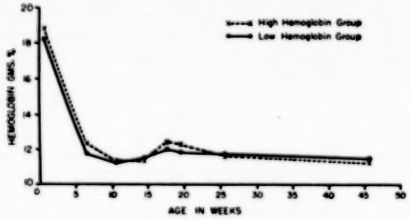


Fig. 9.—Infant hemoglobin determinations.

tioner alike have tended to overlook, in terms of maternal nutrient needs, the demands of lactation and associated maternal factors.

Certainly the mother's activities are increased. In addition, she must provide large amounts of protein, carbohydrates, minerals, and vitamins, as well as calories, for her suckling infant. These demands must be met by the mother's food sources or body stores. If her dietary intake is not adequate, it is to be expected that some weight loss will occur. Here is a period that requires a great deal more attention by nutritionally minded physicians—general practitioner, obstetrician, and pediatrician.

At the time of discharge from the hospital, 71% of the mothers in our studies were breast-feeding their infants as compared with the national estimate of 65 to 80% of the mothers. Insufficient milk was the commonest cause given for complete or partial supplementation. Nursing increased with parity and decreased among primiparas over 25 years of age and among mothers less than 85% of standard weight. There was more nursing among women with higher levels of intake of calcium, phosphorus, and riboflavin and more artificial feeding among mothers who had received calcium supplementation. These groups reflected differences in milk consumption between those who nursed and those who did not nurse their infants, since mothers who stated they drank fewer than three glasses of milk per day had a higher frequency of calcium supplementation.

Clear biochemical evidence of lactational demand was shown by the lowered postpartum serum vitamin C levels among the mothers who nursed their offspring (fig. 3). This was not dependent on the nutrient intake of ascorbic acid, since it occurred with all intake levels. When the nutrient intake was above 80 mg. per day, the postpartum serum levels could be maintained at approximately 0.3 mg. per 100 ml. This is in contrast to the serum vitamin C levels of 0.6 to 0.8 Gm. during gestation, with the same level of dietary intake.

Detailed analyses of the relationship of various obstetric and pediatric complications to varying levels of nutrient intake and biochemical measurements on maternal nutriture have been recorded previously.[9] In summary, we can say that for our patients nutritional deficiency does not emerge as a primary causative factor in any of the metabolic diseases of pregnancy that are of unclear etiology. The obstetrician who assures his patient freedom from such complications as toxemia and prematurity by advocating an abundant nutrient intake must expect disappointment. However, we do not wish to be interpreted as concluding that nutrition is unimportant in pregnancy. The necessity of insuring an adequate dietary during pregnancy is unquestioned.

Nutrient Requirements in Reproduction

The target level of nutrient intake during the reproductive interlude may not be defined within a narrow range, since it is dependent upon factors such as activity demands, initial weight status, and stage of gestation. It would be unrealistic to allow three women, each 5 ft. 4 in. tall but weighing 100, 122, and 180 lb. (45.4, 55.3, and 81.6 kg.), respectively, to gain the same amount of weight during pregnancy and to recommend the same nutrient intake. In the following discussion, we shall direct our attention to the mean patient from our study—the woman who is neither underweight nor overweight for her height and body build.

Is there evidence that improved nutrition could be expected to prevent the occurrence of gestational complications? In an effort to answer this question, we have examined the groups at the extremes of dietary intake (table 4). The limits of high and low extremes of nutrient intakes were chosen as greater than one or two standard deviations above or below the mean or median values. Two general deductions are pertinent. 1. A more abundant nu-

trient intake as estimated by caloric level was not associated with a decrease or increase in fetal or obstetric complications, with differences in birth weight or length of the infant, or with physical or biochemical changes (table 5). Similar findings were obtained when the intake estimates were grouped on a basis of protein. 2. When the mother's intake was less than 1,500 calories or less than 50 Gm. of protein, positive correlations were found between certain obstetric and fetal complications and dietary intake during the third trimester. However, the observed increase in incidence of these obstetric and fetal conditions appeared to be responsible for the lowered intakes and not vice versa.[92]

Keeping in mind the modern woman's desire to remain trim, her living pattern, the apparent reduced activity of the expectant mother during the third trimester, the physician's desire to limit weight gain, and the nutritional demands of both mother and infant, this study does not provide evidence to indicate that dietary intakes greater than the average reported or greater than the allowances of the National Research Council will bestow protective benefits during pregnancy. A dietary that will provide the recommended levels of nutrients is readily attainable from food sources in all sections of the country without the need of supplementation. During lactation, on the other hand, less extensive evidence clearly indicates an enhanced caloric expenditure or loss of nutrients for the nursing mother.

We realize that prophylactic broad-spectrum supplementation is commonly prescribed for both private and clinical obstetric patients throughout the country. We use the word "supplement" meaning "to add to, to bring up to adequate levels," rather than "therapeutic." An examination of the label of reputable prenatal preparations shows that the manufacturer's suggested daily dosage will provide from two to five times the National Research Council's recommended allowance for the individual minerals and vitamins. The general routine use of such dosages is extravagant, needless medication. When the obstetrician is concerned that his patient is not obtaining from food sources amounts of minerals and/or vitamins equal to the National Research Council's recommended allowances, simple dietary instruction will usually be corrective. Failing this, supplementation should be aimed at a level that will bring the individual up to the recommended allowances.

Except among women with iron deficiency anemia, we have been unable to find any significant difference in the incidence of maternal or fetal abnormalities or in the clinical nutritional assessment of the groups who received supplements (iron, calcium, or vitamin B complex) and the groups who did not receive supplements. In this instance, as would be true with any nutritional deficiency disease of demonstrable etiology, supplementation is of undisputed value. A less clear situation is present with ascorbic acid nutriture. Although it is apparent

TABLE 4.—*Approximated Nutrient Intakes, Means or Medians, and Ranges, of Any Trimester**

Nutrient†	−2 S.D.	−1 S.D.	Mean	+1 S.D.	+2 S.D.
Total calories	1,000	1,500	2,100	2,750	3,250
Protein, Gm.	40	50	72	90	110
Calcium, Gm.	0.25	0.75	1.10	1.50	2.00
Iron, mg.	6	10	13.5	18	22
Thiamine, mg.	0.7	1.0	1.4	1.9	2.2
Riboflavin, mg.	0.5	1.5	2.5	3.5	4.5
Niacin, mg.	4.0	8.0	12.0	16.0	20.0
	2½%	16%	Median	84%	97½%
Vitamin A, I.U.	1,000	3,000	6,000	11,000	19,000
Vitamin C, mg.	20	40	60	100	160

* Ranges are 1 or 2 standard deviations above or below mean or median equivalents.
† Values are rounded to fit interval groupings of coded material.

TABLE 5.—*Comparison of Third Trimester Caloric Intakes With Third Trimester Laboratory Levels**

Cases with diet records, no.†	Daily Caloric Intake <1,500: 330	1,500-1,999: 555	2,000-2,499: 443	2,500-2,999: 221	>3,000: 116	Total: 1,665
	Means					
Hemoglobin, Gm./100 ml.	11.71	11.77	11.62	11.67	11.70	11.70
Red blood cells, million/cu. mm.	3.95	3.98	3.95	3.94	3.98	3.96
Packed cell volume, %	35.5	35.6	35.5	35.2	35.9	35.5
Mean cell volume, cu. μ	90.4	90.1	90.3	89.7	90.7	90.2
Mean cell hemoglobin, micromicrogram	30.2	30.1	30.1	30.1	30.2	30.1
Mean cell hemoglobin concentration, %	33.6	33.5	33.4	33.6	33.5	33.5
Total serum protein, Gm./100 ml.	6.31	6.34	6.30	6.36	6.36	6.33
Serum albumin, Gm./100 ml.	3.98	4.05	4.04	4.04	4.09	4.03
Serum vitamin A, I.U./100 ml.	101.0	102.0	100.0	98.0	102.0	100.8
Serum carotene, mcg./100 ml.	159.0	159.0	159.0	156.0	162.0	161.2
	Medians					
Serum vitamin C, mg./100 ml.	0.351	0.344	0.368	0.371	0.360	0.356
Thiamine excretion, mg./2 hr.	0.087	0.089	0.094	0.098	0.091	0.091
Riboflavin excretion, mg./2 hr.	0.705	0.735	0.781	0.699	0.760	0.740
N'-methylnicotinamide excretion, mg./2 hr.	10.0	9.5	9.9	9.4	10.4	9.74

* Laboratory levels for given caloric groupings.
† Laboratory values missing in approximately 2% of cases.

that one can maintain serum vitamin C levels during the prenatal period with intakes above 80 mg. per day, some postpartum decline occurring as a result of lactation cannot be prevented. If it is protective to keep serum levels up and if food sources do not provide 80 to 100 mg. of vitamin C, it may be desirable to provide supplements.

Summary

Observations on a total obstetric clinical population have been made. We believe that the findings of this study are widely applicable. Alterations in the patterns of dietary intake and biochemical values during the reproductive interlude revealed fundamental physiological changes in the pregnant and lactating mother. There was a decrease of approximately 200 calories in the average intake between the second and the third trimester. This was associated with a similar decrease in the consumption of most of the individual nutrients.

The change in blood constituents fell into four patterns: (1) a decline during the first 32 to 34 weeks of gestation followed by a postpartum rise; this was present for the mean hematological values, total serum protein, and serum vitamin A, and the urinary excretion of thiamine and riboflavin; (2) a progressive increase during pregnancy followed by a postpartum decline; this pattern was exhibited by serum carotene, tocopherol, and the urinary excretion of N'-methylnicotinamide; (3) a slight decrease in the mean serum vitamin C levels during gestation followed by a further sharp decline post partum among lactating mothers; and (4) a progressive increase in the absorption and utilization of iron as pregnancy advances.

The effects of underweight and overweight, maternal low hemoglobin levels, and lactation on maternal nutriture are described in relation to obstetric and pediatric performance. From conception through parturition and lactation, maternal nutrition should provide adequate amounts of those nutrients that are essential for the mother's maintenance and the growth and development of the fetus. From the present study, it is clear that dietary intakes, greater than the Recommended Dietary Allowances of the Food and Nutrition Board, will not bestow protective benefits during pregnancy. It appears that the recommended standards for calories are too high for the expectant mother of today. A dietary that will provide the essential nutrients is readily attainable from food sources. The common obstetric routine of broad-spectrum nutritional supplementation is questioned, both as to need and as to dosage level. It is apparent that, for the effective use of supplements, the physician must understand the normal physiological changes associated with the reproductive interlude.

This study was supported by grants from the Nutrition Foundation, Inc., the International Health Division of the Rockefeller Foundation, the U. S. Public Health Service, the Tennessee Department of Public Health, and Distillation Products, Inc.

Tables 1 and 2 and figure 5 are reproduced with permission from *Obstetrics and Gynecology.*[9f] Table 4 is reproduced with permission from *American Journal of Obstetrics and Gynecology.*[9d] Table 5 is reproduced with permission from *Journal of the American Dietetic Association.*[9e] Figure 4 is reproduced with permission from *American Journal of Obstetrics and Gynecology.*[5] Figure 9 is reproduced with permission from *Pediatrics.*[8]

References

1. Food and Nutrition Board: Recommended Dietary Allowances, Publication 302, National Academy of Sciences, National Research Council Report, 1953.

2. Ebbs, J. F.; Tisdall, F. F.; and Scott, W. A.: Influence of Prenatal Diet on Mother and Child, J. Nutrition **22**:515-526 (Nov.) 1941. Burke, B. S.; Beal, V. A.; Kirkwood, S. B.; and Stuart, H. C.: Nutrition Studies During Pregnancy, Am. J. Obst. & Gynec. **46**:38-52 (July) 1943. Tompkins, W. T.; Mitchell, R. M.; and Wiehl, D. G.: Maternal and Newborn Nutrition Studies at the Philadelphia Lying-In Hospital, Annual Conference of the Milbank Memorial Fund, New York, 1955.

3. Youmans, J. B.; Patton, E. W.; and Kern, R.: Surveys of Nutrition of Populations: Description of Population, General Methods, and Procedures, and Findings in Respect to Energy Principle (Calories) in Rural Population in Middle Tennessee, Am. J. Pub. Health **33**:58 (Jan.) 1943. Swanson, P., and others: Food Habits of Women 30-90 Years Old, Fed. Proc. **11**:457 (March) 1952. Clark, F., and Finder, L. J.: Nutrition Control of Homemakers' Meals, U. S. D. A. Agric. Inform. Bull. **112**:3, 1954.

4. Martin, M. P.; Bridgforth, E. B.; McGanity, W. J.; and Darby, W. J.: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: X. Ascorbic Acid, J. Nutrition **62**: 201-224 (June) 1957.

5. Hahn, P. F., and others: Iron Metabolism in Human Pregnancy as Studied with the Radioactive Isotope Fe^{59}, Am. J. Obst. & Gynec. **61**:477-486 (March) 1951.

6. McGanity, W. J., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: V. Description and Outcome of Obstetric Sample, Am. J. Obst. & Gynec. **67**: 491-500 (March) 1954.

7. Strauss, M. B.: Anemia of Infancy from Maternal Iron Deficiency in Pregnancy, J. Clin. Invest. **12**:345-353 (March) 1933.

8. Woodruff, C. W., and Bridgforth, E. B.: Relationship Between Hemogram of Infant and That of Mother During Pregnancy, Pediatrics **12**:681-685 (Dec.) 1953.

9. (*a*) Darby, W. J., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: I. Background, II. Methods, III. Description of Sample and Data, J. Nutrition **51**:539-565 (Dec.) 1953. (*b*) Darby, W. J., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: IV. Dietary, Laboratory, and Physical Findings in 2,129 Delivered Pregnancies, ibid. **51**:565-597 (Dec.) 1953. (*c*) Ferguson, M. E., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: VII. Tocopherol in Relation to Pregnancy, ibid. **55**:305-321 (Feb.) 1955. (*d*) McGanity, W. J., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: VI. Relationship of Obstetric Performance to Nutrition, Am. J. Obst. & Gynec. **67**:501-527 (March) 1954. (*e*) McGanity, W. J., and others: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: VIII. Some Nutritional Implications, J. Am. Dietet. A. **31**:582-588 (June) 1955. (*f*) Darby, W. J.; Bridgforth, E. B.; Martin, M. P.; and McGanity, W. J.: Vanderbilt Cooperative Study of Maternal and Infant Nutrition: IX. Some Obstetric Implications, Obst. & Gynec. **5**:528-537 (April) 1955. (*g*) Reference 4.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

Editor . . . . . JOHNSON F. HAMMOND, M.D.
Assistant Editors . . . . . WAYNE G. BRANDSTADT, M.D.
FREDERIC T. JUNG, M.D.
Assistant to the Editor . . . . . MILTON GOLIN
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.
News Editor . . . . . CHARLES CHAPMAN

Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

PREVENTIVE MEDICINE

AT ONE TIME, preventive medicine was synonymous with public health. Nowadays it is an integral part of total medical care. Not so long ago, preventive medicine was thought to be limited to sanitation and other forms of environmental and regulatory control. Today the term prevention in medicine applies not only to immunizations but to the avoidance of sequelae and recurrence as well as the prevention of communicability.

Communicability is not limited to contagion. The personal physician must prevent the spread of symptom-complexes to other members of the family. He must prevent seemingly unrelated ill-effects on persons associated with the patient. These ill-effects may arise merely because of the cultural and environmental changes associated with having a sick person around, although they have no direct connection to the specific illness. Lastly, the physician must be interested in adverse effects—economic, social, and especially emotional—that can arise as side-effects of being sick.

How much time can a physician spend doing preventive medicine, when his patients demand so many of his curative skills? The answer to such a question might be as much as the immediate care of the sick will allow. But, if the factor of health promotion is considered rightfully as part of the prevention of disease, the average practitioner spends a great deal more time and effort than the public, or even he himself, supposes.

There are many concepts to consider in the practice of preventive medicine. Primarily, there is the aspect of patient acceptance. Secondarily there is the matter of what diseases or illnesses can be prevented. In the first instance, how many people, in apparent good health, seek out their family physician strictly for the purpose of maintaining their "well" state of being? A survey conducted seven years ago implied that only 5 out of every 100 patients seeking medical care or advice were primarily interested in preventing future disease. The remainder had acute (to the patient) medical problems requiring immediate and specific care. After such care the patient usually declines to continue having medical attention.

As to the matter of which diseases offer applicable preventive techniques, it might be said that wherever the etiology is known, or even suspected, there eventually will be a means of avoidance. Other than communicable (micro-organism) diseases, such generalizations include nutritional illnesses, allergic manifestations, occupational conditions, accidents, and certain psychiatric syndromes, to name but a few.

Many physicians have tried to entice well patients to have their eyes examined for glaucoma, to have their urine tested for diabetes, or in the past, before x-rays became secondary to tuberculin testing as a case-finding procedure, to have a "free" chest examination. Who takes advantage of such preventive techniques? Too often, not the man who is coughing. Nor the person whose mother had diabetes. Nor the woman who is having difficulty seeing. These people, like so many others, seem to be more afraid of learning something is wrong than they are of preventing serious consequences. They have been taught, through publicized advances of medical science, that there would be a cure should the disease ever really take hold. Fear of finding out is greater than the publicized fear of actually having a malady.

A physician cannot force any form of medical care on the public. While some legislative acts require utilizing various preventive practices, such acts do not project their over-all value in terms the average person can understand. The recent laxity in poliomyelitis immunizations seems to confirm this point of view. Perhaps a future job will be to promote the idea of total medical care on a personal basis, to include seeking preventive medical care from the physician's office. Every disease or illness that is prevented allows that much more time to devote to the sick.

THE GENERAL PRACTITIONER'S AWARD

The House of Delegates of the American Medical Association at the 12th Annual Clinical Meeting in Minneapolis on December 2 named Dr. Lonnie A. Coffin of Farmington, Iowa, the general practitioner of the year. He was presented with a gold medal and citation by Dr. Gunnar Gundersen, President of the American Medical Association. Dr. Coffin, who is the first Iowan to receive this honor, was born on a farm in Clark County, Missouri, in 1890 and moved to Iowa at the age of 5. He was a member of the last medical class to be graduated from Drake University in Des Moines. After a year of internship at Iowa Methodist Hospital in Des Moines he established a general practice in Farmington. Except for two years of military service in World War I he has served his community continuously for 44 years. Mrs. Coffin died last year, but he is fortunate in having two married daughters, both living in Farmington, and four grandchildren.

LONNIE A. COFFIN, M.D.

Although his practice keeps him busy, he has taken time for civic affairs, serving on the school board for 15 years, serving two terms on the city council, and taking an active part in the local post of the American Legion of which he was the first commander. In addition to being a member of the county and state medical societies and the American Medical Association, he is a member of the local Chamber of Commerce and the Iowa Academy of General Practice. He has served on the board of trustees of the Iowa State Medical Society and was its president in 1956. Although he calls himself just an ordinary country doctor his patients refuse to accept this designation. Their esteem for him was summed up by one who said, "There might be doctors who have done just as good and just as much—but none has done more any better."

LET US PUT AMEF "OVER THE TOP"

It is gratifying to learn that during 1957 the medical profession contributed more than four million dollars to medical education. Nearly one million dollars was contributed through the American Medical Education Foundation, with the balance consisting of direct grants or gifts to the schools or through their alumni organizations. In recent years there has been a steady increase in the number of physicians giving such financial assistance to the schools as well as in the total amounts made available through the American Medical Education Foundation or by direct gifts.

This is the time of year when final decisions must be made by all in regard to tax deductible contributions for 1958. There are only a few days left in which it is possible to make a gift in support of medical education through AMEF that will aid in bringing the contributions from the profession for 1958 to a new record. In order to achieve this new goal in support of the medical schools and for your convenience, THE JOURNAL has bound an envelope in the advertising pages in the back of this issue.

Please write out a check for your gift to medical education through the American Medical Education Foundation and forward it today in this envelope. Let us complete 1958 with a record support of medical education by the medical profession, a matter of professional pride, and a genuine challenge to others.

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

ORGANIZATION SECTION

HIGHLIGHTS OF 12TH CLINICAL MEETING

Bold approach and action to bring improved medical care within the reach of more and more older persons highlighted House of Delegates actions early this month at the American Medical Association's 12th Clinical Meeting. The A. M. A. policy-making body of 198 Delegates made its stand clear through reports and resolutions (among 19 considered) covering aspects of low family income, indigent care, prepaid health insurance, "relative value schedules," and medical care plans. While all of these points reflect the medical profession's concern for personal health generally, the House actions in Minneapolis Dec. 4 showed a distinct emphasis on the health needs of a growing population of aged persons.

In other significant fields, the Delegates expressed their views on federal medical services, disaster preparedness, osteopathy, the "free choice of physician" principle, expansion of medical education facilities, and a re-examination of A. M. A. objectives and basic programs. Dr. Gunnar Gundersen of LaCrosse, Wis., President of the A. M. A., sounded the keynote for the meeting in his opening address Dec. 2 when he said:

> While we fight hard to preserve basic principles and objectives which are essential to good medical care, we also must be alert and adaptable to the changing times in which we live. . . . The time has passed for policies based on generalities, platitudes and flag-waving. The time has passed for medical crankiness, complaint, arrogance and pigheadedness—wherever they might exist. The time has passed when we can fight our battles simply by quoting George Washington, Thomas Jefferson and the rest of the founding fathers. . . .

Following Dr. Gundersen on the rostrum, Minnesota Governor Orville L. Freeman told the Delegates:

> You certainly have the right to oppose [Forand-type] legislation if you believe it would be harmful to your profession. You have the duty to oppose it if you believe it would be harmful to the public. But if you do oppose it you also have the responsibility of helping to work out an alternative program to meet the need that we all know exists and becomes more serious every day. . . . Senior citizens need better care.

Scope of Meeting

The year-end Clinical Meeting is designed to help the family physician meet his daily practice problems. This was accomplished in the Minneapolis Auditorium through reports from nearly 200 experts in various fields of medicine who brought him up to date on rapidly changing developments—and through 100 scientific exhibits, 130 technical exhibits, closed-circuit medical television (on a 9 by 12 ft. color screen), motion pictures, lectures, and panel discussions (including a conference via under-sea telephone cable with physicians in Southampton, England). The A. M. A. met previously in Minneapolis in 1928.

Registration included 2,658 physicians and 2,561 medical students, nurses, technicians, and guests—for a total official attendance of 5,219.

The General Practitioner of the Year award was presented to Dr. Lonnie A. Coffin, aged 68, of Farmington, Iowa. Except for two years of military service during World War I, he has been a key figure in his community for 44 years—delivering 2,500 babies (including 2,000 in the home), leading in civic and recreational activities, serving on the city council and the local school board, and playing vigorous roles in religious, veteran, and medical society affairs.

Earlier issues of THE JOURNAL carried some advance reports of the Clinical Meeting as well as brief statements of Trustees and officers. Future issues will contain an abstract of the proceedings, which eventually will be presented fully in pamphlet form. Following are summary high points of House of Delegates actions:

Oldsters, Fees, Insurance

The House adopted a report from its Council on Medical Service, urging that:

> . . . physicians everywhere expedite the development of an effective voluntary health insurance or prepayment program for the group over 65 with modest resources or low family income; that physicians agree to accept a level of compensation as full payment for medical service rendered to this group, which will permit the development of such insurance and prepayment plans at a reduced premium rate. This recommendation has been studied and restudied by the Board of Trustees and has received its wholehearted endorsement.

In a related action, the House decided to face the "very important problem" of relative value studies. Relative value studies are not fee schedules. Rather, they are attempts to show (by unit or point designation) the relationship between time, competence, effort, experience, and other factors required to perform one professional service as compared with those required for other professional services. In accepting a Committee on Medical Practices report calling for relative value studies, the House of Delegates agreed that:

> Unless medicine does undertake this activity, it may be done by others who are less qualified. . . . The House of Delegates approves in principle the conducting of relative value studies by each constituent medical association rather than a nationwide study or series of regional studies. . . . The nomenclature, descriptions and code numbers of the California Relative Value Study (almost identical with those of Kansas and Iowa) can well be accepted as a national format. . . . No unit values and/or dollar values are to be used or suggested.

The Delegates adopted a resolution authorizing the Council on Medical Service to sponsor "at the earliest practicable date" a Congress on Prepaid Health Insurance where plans may be formulated for "offering sound and constantly improving voluntary health insurance to the citizens of our nation." The House also approved a set of "Suggested Guides for Medical Society Sponsored Voluntary Prepayment Medical Benefit Plans."

On the matter of prepaid health insurance for elderly persons, the Delegates accepted a reference committee report which noted that Blue Shield Medical Care Plans "presently have a special committee studying seven distinct approaches to this problem. Many private insurance companies are also removing the 65-year age limit for benefits."

The House also recommended that Congress amend the Social Security Act to permit states to combine the present four public assistance medical programs into a single one.

Medical Care Plans Report

The long-awaited report of the 15-member Commission on Medical Care Plans was received without discussion on the floor of the House, although discussion at a reference committee hearing lasted for two hours. In deciding to defer action on the three and one-half year study until the Annual Meeting in Atlantic City next June, the Delegates noted that "the weight of testimony" in reference committee hearings "indicated that many members had not had an opportunity to study the report and, therefore, were unable to render an opinion at the present time." The House directed that, meanwhile, the Board of Trustees invite state medical associations to reply (by April 8 to Executive Vice-President F. J. L. Blasingame at A. M. A. headquarters in Chicago) to the following questions:

1. Acknowledging the importance of free choice of physician, is this concept to be considered a fundamental principle, incontrovertible, unalterable, and essential to good medical care without qualification?
2. What is or will be your attitude regarding physician participation in those systems of medical care which restrict free choice of physician?

The Commission suggested a definition of "freedom of choice" as "the right of the individual to exercise, without restraint, selection among alternatives." The Commission report adds: "The medical profession subscribes to, supports, and strives to attain complete acceptance and application of this principle of freedom of choice." The Commission's suggested definition of third parties was "mechanisms which, for any reason, enter into the relationship between the patient and his physician."

In its long study, the Commission on Medical Care Plans has explored the operation of various types of plans through which persons receive the services of physicians, the effect of these plans on quality and quantity of medical care, and the legal and ethical status of arrangements used by various plans.

Aleson Committee Report

The House accepted two recommendations, disapproved a third, and modified a fourth recommendation of its Committee to Study A. M. A. Objectives and Basic Programs. The Delegates also agreed with the special Committee, headed by Dr. Lewis Aleson of Los Angeles, that it should be disbanded. The Committee was appointed a year ago to modify recommendations which had their origin in the findings of a management consultant firm. Recommendations adopted this month in Minneapolis were that the Board of Trustees "give serious consideration to opening the publications of the Association to a free and open discussion of socioeconomic problems applicable to medicine" and that consideration be given to amending Article II of the A. M. A. constitution with the following substitution:

The objectives of the Association are to promote the science and art of medicine and the betterment of public health and an understanding of the socioeconomic conditions which will facilitate the attainment of these objectives.

The Aleson Committee recommendation which was disapproved dealt with the proposed creation of a Council or Committee on Socioeconomics for a three-year period. The House decided this would not be necessary in the light of plans already under way to develop such a division based at A. M. A. headquarters.

Although the House accepted an Aleson Committee recommendation that the Board of Trustees "establish a mechanism which will assume the responsibility for promoting active liaison with each national medical society," a subsequent sentence was modified to read:

In the scientific fields the role of the A. M. A. *should be primarily that of leadership*, but every endeavor should be made to bring about coordination of the special fields of scientific interest of the other national medical organizations.

Other House Decisions

The House of Delegates also made decisions on the following topics:

Fund Solicitations—Adopted a resolution requesting the Board of Trustees to arrange a "top-level conference" with voluntary health agencies, the United Funds, and other parties interested in the raising of funds for health causes—with the view of resolving "misinterpretations and other difficulties in this area."

Administrative Reorganization—Accepted and praised a Board of Trustees report which detailed a reorganization of the Headquarters staff into seven divisions and which noted that "extra effort is being made to coordinate the activities in the Washington and Chicago offices, and the over-all direction will come from Chicago."

Licensure of Paramedical Groups—Went on record as encouraging the voluntary registration of persons in fields allied to medicine who assist physicians, and opposed the extension of governmental licensure and governmental registration.

Osteopathy—Disapproved a resolution which would establish the sovereignty of relationships between medical societies and the osteopathic profession in their respective states. At the same time, the Delegates asked the Judicial Council to report next June, if possible, on past pronouncements of the House with respect to osteopaths and applicable state laws.

Amphetamines and Athletes—Authorized the Board of Trustees to allow continuation of a Committee study of this subject "in view of the complexity of the problem" and to submit a final report at the Atlantic City meeting.

Civil Defense—Adopted a resolution urging that:

—The A. M. A. recommend that discussions "be started with the view to developing a plan whereby reserve units and individuals can be used to supplement civil defense operations."

—Consideration be given "for the rapid training of civilians" to fill the places of medical reservists.

—A plan be explored for the recruitment, training, and use of former medical personnel who have no further military obligation "so that their services may be utilized for civil defense purposes."

Service Membership—Adopted a resolution of the Council on Constitution and Bylaws, urging that all county medical societies "make every effort" to provide a type of membership for armed forces, Public Health Service, and Veterans Administration physicians which will enable them to become active members of state medical associations and the A. M. A.

Social Security for Physicians—Recognized a resolution indicating that 45.7% of the membership of the Ohio State Medical Association replied "yes" last October to a survey question, "Should physicians be included in the federal social security program?" The House voted that detailed results of the poll be transmitted to the A. M. A. Board of Trustees "for its information and for the information of any of the Councils or Committees of the Association concerned with this matter."

Medicare—Noted curtailment of this federal program and recommended that "the A. M. A. encourage the re-establishment of services under the free choice principle to accomplish the original intent of the Medicare Act."

Poliomyelitis—Endorsed a Board of Trustees report called for renewed public education efforts to secure the minimum of three poliomyelitis vaccine injections.

Korean Children in U. S.—Urged that the Public Health Service, the State Department, and Congress be alerted that some Korean children adopted in the United States are suffering from communicable diseases which are antibiotic resistant and "increase the seriousness of this public health threat."

International Medical Year—Expressed support for a proposed International Medical Year, similar in purpose to the International Geophysical Year.

Commendation of Dr. Austin Smith—Heard Dr. John Galbraith of New York introduce the following resolution:

WHEREAS, The House of Delegates of the American Medical Association has learned with great regret of the resignation of Dr. Austin Smith as Editor of THE JOURNAL of the American Medical Association; and

WHEREAS, Dr. Smith has rendered outstanding service both to the American Medical Association and to the American public, in his former capacities as Secretary of the Council on Pharmacy and Chemistry, as Director of the Division of Research and more recently as Editor; and

WHEREAS, the scientific activities of the American Medical Association are its most important functions; and

WHEREAS, a scientist of the caliber of Dr. Smith will be most difficult to replace, therefore be it

Resolved, by the House of Delegates of the American Medical Association assembled in Minneapolis December 2 to 4, 1958, that it expresses to Dr. Smith, first its sincere regret at his resignation; second, its gratitude and appreciation for his long years of devoted, loyal and efficient service; and third its best wishes to him for long life, health and happiness; and be it further

Resolved, that this resolution be spread upon the minutes of the meeting, published in THE JOURNAL of the American Medical Association and a copy be sent to Dr. Smith.

Other Meeting Highlights

The Board of Trustees appointed Dr. W. Linwood Ball of Richmond, Va., as a Trustee for six months, to temporarily fill the vacancy created by the death last Nov. 19 of Dr. Warren W. Furey of Chicago. Dr. Ball will also continue to serve as A. M. A. Vice-President.

A conference on Federal Medical Services Dec. 1 covered such topics as medicare, education and research in veterans' medical care, and the future of Hometown Care Programs for veterans.

In a brief ceremony before the opening session of the House of Delegates, the American Medical Education Foundation received checks totaling $248,659. Later, the A. M. A. added its contribution of $100,000.

DR. AUSTIN SMITH RESIGNS

Dr. Austin Smith, Editor of THE JOURNAL since Dec. 1, 1949, has tendered his resignation and it was accepted by the Board of Trustees, effective Dec. 15th. Dr. Smith had served also as director of editorial policies for the A. M. A.'s nine monthly specialty journals. He joined the American Medical Association in February, 1940, as a medical consultant. In September, 1942, he was made secretary of the Council on Drugs and in 1946 was named, also, director of the Division of Therapy and Research.

Dr. F. J. L. Blasingame, the Executive Vice-President, said, "The American Medical Association accepts Dr. Smith's resignation with regret and is grateful to him for his many years of service. Every good wish is extended to him in the years ahead."

COUNCIL ON MEDICAL SERVICE

MEDICAL CARE FOR THE INDIGENT IN 1958

On June 15, 1957, the Committee on Indigent Care of the Council on Medical Service published in THE JOURNAL a series of 52 questions and answers concerning current legislation governing medical care programs for recipients of public assistance (old age assistance, aid to the blind, aid to the permanently and totally disabled, aid to dependent children). In October, 1957, and May, 1958, the Committee published Supplementary Reports 1 and 2 to that study, bringing the material up to date in the light of the 1956 and 1957 Social Security Amendments, effective July 1, 1957.

On Aug. 29, 1958, the President approved the 1958 Social Security Amendments (H. R. 13549), which again change the methods of financing and administering public assistance medical care, effective Oct. 1, 1958. The following report is therefore issued to inform the medical profession concerning the federal laws now governing public assistance medical care programs.

Background of Program

1. *How was medical care provided for public assistance clients prior to July 1, 1957?*

The state was free to choose its own method. It could pay for public assistance medical care from public assistance funds, with limited federal participation in the cost, either as part of the money payment to the assistance recipient or, since 1950, through payments to the providers of medical services—"vendor payments." ("Medical services" is interpreted to include physicians and hospitals, nursing homes, pharmacists, dentists, and other auxiliary health services.) The state could also, if it so desired, provide medical services for its indigent entirely from state and local funds, using all the federally matched public assistance funds for money payments to the assistance recipients for their other basic needs.

2. *How did the 1956-1957 amendments, effective July 1, 1957, change this situation?*

The 1956 amendments established a separate matching formula for vendor medical care payments, under which the federal government would reimburse half the state's expenditures, up to a maximum state expenditure of $6 per adult and $3 per child per month (average). All public assistance expenditures for medical care not included within these limits were subject to federal reimbursement only if spent as money payments to the assistance recipients.

The 1957 amendments allowed the states to choose between this formula and the one in effect prior to July 1, 1957 (the effective date of the change).

3. *What were the results of these amendments?*

Almost all states benefited financially from the separate matching formula. However, some states which had established relatively comprehensive medical care programs on a vendor payment basis found that, because of the $6 and $3 limitation, they would have to curtail the vendor portion of their programs to obtain maximum federal participations.

Other states, in order to obtain the additional federal funds "earmarked" for public assistance vendor payments, found it necessary to revise their administrative operations.

These amendments and the federal funds authorized did, however, encourage some states having no statewide public assistance medical care program to initiate a formal program for public assistance recipients with encouragement of these federal funds.

A. M. A. Policy

4. *Did the American Medical Association take a position on these amendments?*

In December, 1956, the House of Delegates of the A. M. A. adopted the "Guides for Medical Societies in Developing Plans for Tax-Supported Personal Health Services for the Needy." This policy statement included the recommendation that the methods and amounts of payment for personal health services in such programs should be determined in conference between the responsible state and local government agencies and representatives of the providers. The new formula, by placing restrictions on federal funds for vendor medical care payments and requiring that all other public assistance funds be spent as money payments, in effect limited the state's freedom of decision as to the method of payment. In June, 1958, the A. M. A. House of

Members of the Committee on Indigent Care are Drs. John Flack Burton, Chairman, Oklahoma City; A. J. Bowles, Seattle; I. Jay Brightman, Albany, N. Y.; E. P. Coleman, Canton, Ill.; Wesley W. Hall, Reno, Nev.; E. A. Ockuly, Toledo, Ohio; Dean W. Roberts, Chicago; Mr. R. M. Hilliard, Consultant, Chicago; and Mr. Nelson B. Neff, Consultant, Reno, Nev. Staff members are Mr. George W. Cooley, Secretary, and Mr. James H. Fleming, Research Assistant.

Delegates reaffirmed its 1956 position and advocated the return to the states of all the decisions as to methods of payment.

5. *Are the 1958 amendments in accordance with this A. M. A. policy?*

Yes, insofar as they return to the individual state the decision as to the method of payment of public assistance funds for medical services.

Changes in Law

6. *Do the 1958 amendments merely cancel out the 1956 and 1957 changes in the law?*

No. There are changes in the maximum amounts eligible for federal matching, the method by which the total state expenditure eligible for matching is calculated, and the proportion of the cost to be met by the federal government. Several new items have also been added: Extension of the public assistance programs to Guam (not previously included), the authorization of payments to legal representatives of assistance recipients, and the establishment of a special Advisory Council on Public Assistance comprising representatives of employers, employees, program administrators, specially qualified persons, and the public. (These last two changes will not be discussed here, since information concerning them is insufficient to discuss their medical significance.)

7. *Will any of these changes directly affect indigent medical care programs?*

As the law now stands pending the issuance of any regulation changes by the Bureau of Public Assistance, Social Security Administration, Department of Health, Education, and Welfare, it appears that the medical care situation has been returned to its pre-1957 status. Each state can set up its program to use public assistance funds entirely for money payments, or for both money and vendor payments, with no financial advantage attached to either arrangement influencing its decision. However, since matching changes will probably bring more federal money into the programs in most states, there is a potential increase in the total state expenditures for public assistance which may lead to augmented medical services as well as increases in the basic maintenance budget.

8. *May expenditures still be made for medical care only?*

Yes. The federal law and regulations provide for participation in medical payments for persons who are in the categories covered by these programs and do not need a money payment, but who are eligible for public assistance because of inability to pay for medical care.

Matching Amounts

9. *What changes have been made in the determination of expenditures eligible for federal reimbursement?*

The maximum amount matchable per person has been changed in all four programs, and it is now based on average expenditures rather than on the actual amount expended for each individual.

10. *Is the "maximum amount matchable" the same as the amount of the federal share?*

No. The "maximum amount matchable" refers to the amount of state expenditures to which the matching formulas are applied. The federal government reimburses a portion of this cost; whatever is spent by the state over this limit receives no federal reimbursement.

11. *What is the maximum amount matchable per person under the new legislation?*

The federal government may participate in state expenditures up to a limit of $65 per person per month for recipients of aid to the aged, blind, and disabled, and up to $30 per person per month for recipients of aid to dependent children.

12. *How does this differ from the previous maximums?*

Prior to Oct. 1, 1958, there were actually two matching formulas. Under the basic formula, the federal government shared in the state's monthly expenditures up to a limit of $60 per person in the aid to the aged, blind, and disabled programs and up to a limit of $32 each for one dependent child and the adult responsible for his care and of $23 for each additional dependent child in the same home. Under the vendor medical care payment matching formula, the federal government shared in state expenditures up to a limit of $6 per adult and $3 per child.

If the state chose to utilize both formulas, the basic formula applied to money payments only and the $6-and-$3 formula to vendor payments only; if it did not utilize the $6-and-$3 formula, the basic formula applied to the combined money and vendor payments.

Averaging Provisions

13. *Are the new matching maximums applied to state expenditures in the same way as prior to Oct. 1, 1958?*

No. Prior to Oct. 1, the maximum in the basic formula was applied to each individual's money payment while the $6-and-$3 formula was based on the average vendor payment per person on the assistance rolls. Under the new amendments, all public assistance expenditures in a given program are averaged monthly against the total number of recipients in that program.

For example, under the earlier system, if one old age assistance recipient had a money payment of $40 and a vendor payment of $4 and another had a money payment of $80 and a vendor payment of $8, the money payments could not be averaged, but the vendor payments could if the $6-and-$3 formula were used. Thus, if both formulas were in use, $40 and $60 of the money payments would be eligible for federal matching under the basic formula and $6 and $6 (average of $4 and $8) under the vendor payment formula. If only the basic formula was in use in the state, the amounts eligible for federal matching would be $44 and $60.

Under the current law, all payments would be averaged ($44 plus $88 divided by 2 = $66) and $65 of this average payment would be eligible for matching.

14. *How will this affect the operation of "pooled funds" for medical services?*

For some years, a number of states have operated "pooled funds" set up to distribute medical expenses among all assistance recipients. In this system, a set amount from each recipient's grant is paid into a special fund for medical costs, while payments out of the fund are made in proportion to care provided. Thus, a recipient might receive a money payment of $55 and have $5 paid into the fund in his behalf, so that all expenditures in his behalf would come within the individual $60 maximum—and yet the recipient might have an amount much larger than $5 paid out of the fund for medical services he received.

Since the $6-and-$3 formula for vendor medical care payments was itself based on an averaging of medical expenditures against the total number of assistance recipients in a program, there was less reason for a "pooled fund" in most states utilizing this new formula.

Under the current law, since all public assistance expenditures, both money and vendor payments, are averaged for federal matching, there would appear to be few states which would gain any financial advantage by maintaining a "pooled fund." However, it may possibly provide administrative advantages in some states insofar as it would enable them to separate medical expenditures from other basic maintenance items and, perhaps, maintain a reserve to meet commitments with providers of services. There appears to be no legal obstacle to such a fund and a number of states are planning to continue using this mechanism.

15. *May expenditures under all four programs be combined and averaged against the total public assistance caseload?*

No. The four public assistance programs remain distinct entities, which may even be administered by different state agencies, and separate accounts must be maintained for each. A separate average expenditure must be calculated for each program.

Federal Participation

16. *Does the federal share of public assistance expenditures remain the same as under prior formulas?*

Only in those states which have a per capita income above the national average; in other states, the federal share will increase.

17. *What was the federal share of expenditures prior to Oct. 1, 1958?*

Under previous formulas for aid to the aged, blind, and disabled, the federal government reimbursed ⅘ of the first $30 expended per recipient by the state under the basic formula and ½ the remainder up to the individual matching maximum of $60. If the state also utilized the $6-and-$3 formula, the federal government reimbursed ½ the average vendor payment up to a state expenditure of $6 and participated in only so much of the basic $60 maximum as was made in the form of money payments.

For dependent children, the federal share was 14/17 of the first $17 per recipient plus half the remainder up to the maximums of $32 each for the first child and the caretaker in a home and $23 for each additional child. If the state also utilized the $6-and-$3 formula, the federal share was ½ the vendor medical care payments up to a state expenditure of $3 times the number of children and $6 times the number of adults on the ADC rolls. The basic formula would then apply only to money payments.

18. *How has the federal reimbursement been calculated since Oct. 1, 1958?*

The expenditures in each public assistance program, including both money and vendor payments, are totaled monthly and averaged against those receiving money payments plus those in whose behalf only vendor payments are made during that month. The first part of the formula for determining the federal share remains the same as prior to Oct. 1, 1958: The federal government repays state expenditures at ⅘ of the first $30 per recipient per month (average) in the aid to the aged, blind, and disabled programs, and at 14/17 of the first $17 per recipient of aid to dependent children. The second part of the formula, covering the federal share of average expenditures between $30 and $65 and between $17 and $30, the new maximums, is, however, no longer 50% for each state, but may vary from 50% to 65% of the state expenditure. This varying share is related to each state's per capita income, so that the poorer states receive a proportionately larger federal reimbursement.

19. *In how many states will the federal share be increased by this system?*

The federal government will pay more than the previous 50% in 33 states. In 19 states, it will pay the maximum percentage under the act, 65%.

Percentage of Federal Expenditure, by States, 1958-1961 Period (Promulgated by Secretary of Health, Education, and Welfare)

Alabama	65.00	Nebraska	63.41
Arizona	63.23	Nevada	50.00
Arkansas	65.00	New Hampshire	57.59
California	50.00	New Jersey	50.00
Colorado	53.42	New Mexico	65.00
Connecticut	50.00	New York	50.00
Delaware	50.00	North Carolina	65.00
District of Columbia	50.00	North Dakota	65.00
Florida	59.68	Ohio	50.00
Georgia	65.00	Oklahoma	65.00
Idaho	65.00	Oregon	52.58
Illinois	50.00	Pennsylvania	50.00
Indiana	50.00	Rhode Island	50.00
Iowa	63.23	South Carolina	65.00
Kansas	60.78	South Dakota	65.00
Kentucky	65.00	Tennessee	65.00
Louisiana	65.00	Texas	61.36
Maine	65.00	Utah	65.00
Maryland	50.00	Vermont	65.00
Massachusetts	50.00	Virginia	65.00
Michigan	50.00	Washington	50.00
Minnesota	58.57	West Virginia	65.00
Mississippi	65.00	Wisconsin	54.00
Missouri	53.42	Wyoming	50.92
Montana	54.97		

20. *How is federal participation determined outside the continental United States and in Alaska?*

The law specifies that the federal percentage in Alaska and Hawaii shall be 50%, without regard to the per capita income.

In the Virgin Islands, Puerto Rico, and Guam (included in the program for the first time), federal participation is set at a flat 50% of monthly expenditures up to $35 times the number of recipients of aid to the aged, blind, and disabled, and $18 times the number of aid to dependent children recipients. The law also sets an annual limit on federal reimbursements for these three areas of $8,500,000 to Puerto Rico, $300,000 to the Virgin Islands, and $400,000 to Guam.

Effect on State Financing

21. *How will these new formulas affect the proportion of federal support for state programs?*

It seems probable that the combination of averaging expenditures and increasing federal participation for low income states will mean an increase in federal reimbursement in almost every state. The Bureau of Public Assistance estimates that, if state expenditures continue at their present levels, the increased federal share will amount to about 198 million dollars per year.

22. *Are any states likely to receive less federal reimbursement under the new formula?*

It would be possible, but appears unlikely in most states, since this loss could occur only in high income states which had been making maximum payments to each individual on the rolls.

Future Developments

23. *Has the medical profession taken any stand on increased federal participation in this program?*

No. As previously noted (question 4) the American Medical Association has stated that the method and amount of payment for medical services for the needy should be determined at the state or local level, and in conference with representatives of the providers of such services. In accordance with this policy, the A. M. A. has not found it appropriate to specify any level of funding as necessary or adequate either for indigent medical services or for the entire public assistance program. Such decisions should be made by local authorities on the basis of the local situation.

24. *What is the probable effect of these amendments on indigent medical care programs?*

Two factors may influence the development of such programs: The restored freedom of decision as to allocation of funds for the states, and the increased federal share in the costs in most states. The first factor will allow the individual states to increase or decrease their vendor payment programs as they will, without being influenced by concomitant increases and decreases in federal aid. This may result in the restoration of some vendor payment programs curtailed during the past year. It is unlikely that this freedom will cause the discontinuance of many programs unless there is continued strong local opposition, since few such programs are eliminated once begun.

The second factor, the increase in federal support, may lead to increase in public assistance programs, particularly among the low income states. It is difficult to predict which direction such increases may take, since there is pressure on some of these states to provide a more adequate payment to meet basic nonmedical costs. However, the greatly increased interest in medical care programs among state and local government officials generally, and among welfare officials in particular, may mean some increase in this type of service to the indigent.

Further Information

Since the Social Security Amendments of 1958 did not become law until Aug. 29, 1958, to become effective Oct. 1, 1958, there has, as yet, been little time for program planning by the various states. The Committee on Indigent Care of the Council on Medical Service will continue to report on significant changes as they occur; those desiring further information should write to the Council office, 535 North Dearborn Street, Chicago 10, Illinois.

NOTE: The 1958 amendments also affect the OASDI and Maternal and Child Welfare programs; changes in these programs are not included in this report.

MEDICAL NEWS

ARKANSAS

Dr. Riggin Wins Award.—Dr. John T. Riggin, associate dean of the University of Arkansas School of Medicine, Little Rock, has been given the first annual award of the Arkansas Conference of Tuberculosis Workers "for outstanding work in the control of tuberculosis in the state." He was given a plaque signifying his achievements and those of his colleagues in the establishment and operation of a chest clinic at the University Medical Center and for other statewide activities in the management of tuberculosis. The clinic, organized in July, 1956, provides a means for diagnosing and evaluating patients with suspected tuberculosis and gives outpatient clinic treatment to those not hospitalized in sanatoriums. The clinic provides follow-up care of patients released from sanatoriums and provides the mechanism for training medical students in the diagnosis and treatment of tuberculosis. Dr. Riggin reported that the clinic treated 876 patients in the first two years of its operation. Of these, 99 were referred and/or admitted to either the Booneville or McRae State Tuberculosis Sanatoriums. Another estimated 100 patients were given outpatient therapy at the Medical Center. The clinic sees only indigent patients except in those instances when private physicians refer patients to the Medical Center for specific diagnosis or treatment.

CALIFORNIA

Dr. Rytand Named Bloomfield Professor.—Dr. David A. Rytand was named the first Bloomfield Professor of Medicine at Stanford Medical School. The appointment was revealed at a Big Game reunion luncheon for medical alumni marking the school's 100th anniversary. The professorship honors Dr. Arthur L. Bloomfield, emeritus professor of medicine, who retired in 1954 and who is now engaged primarily in adding to his writings on internal medicine.

School of Medicine Consolidates in San Francisco.—For the first time since the earthquake and fire of 1906, the whole University of California School of Medicine is located at the University of California Medical Center, San Francisco. The freshman medical students who enrolled were the first to receive their basic instruction in anatomy, biochemistry, and physiology in the new, 14-story second unit of the Medical Sciences Building on the San Francisco campus. The first-year courses previously were given on the Berkeley campus, and the departments that teach them completed their move to San Francisco during the summer. This move permits the entire medical curriculum to be offered on a single campus and has made possible an increase from 78 to 100 in the first-year class. It also provides teaching and research space for other Medical Center departments, and it houses the Medical Center Library, and auditorium, and an animal tower. The new unit also provides additional teaching and research space for the School of Pharmacy, the division of oral biology of the School of Dentistry, the Cancer Research Institute, and the departments of medicine, microbiology, parasitology, pathology, pharmacology, and radiology in the School of Medicine. About 176,000 square feet of floor space are housed in the new Medical Sciences unit, which cost $5,773,649. Construction began in 1955. Another major teaching and research building is scheduled for construction beginning in 1960. To be called the Health Sciences Instruction and Research Building, it will extend toward Mt. Sutro from the rear of the Medical Sciences Building. The 10-million-dollar structure is designed to help many Medical Center departments.

COLORADO

Emergency Hospital Unit for Civil Defense.—A 200-bed civil defense emergency hospital was received by the University of Colorado Medical Center, Denver, from the federal government to expand facilities in the event of a civilian disaster and to serve training and educational purposes. Robert L. Denholm, Colorado University Medical Center administrator, said the unit weighs 13 tons and consists of more than 400 separate items. Delivered Nov. 17, the unit will be stored at the Medical Center and will be used to familiarize medical, nursing, and other personnel with its use. In the event of a civilian disaster, the hospital will be set up at the Medical Center and used on a temporary basis. The equipment received includes: a 15-kilowatt generator, a 1500-gallon nylon water storage tank and pump, three operating rooms, a clinical laboratory, x-ray facilities, a sterilizing unit, pharmacy, and central supply room.

CONNECTICUT

University News.—Dr. Kenneth D. Keele, consultant physician at the Ashford Hospital, Middlesex, England, was appointed visiting professor of the

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

history of medicine at the Yale School of Medicine, New Haven, and will be at Yale from October through December. He will work with Dr. John F. Fulton, Sterling Professor of the History of Medicine, in teaching medical and other university students in history of medical research. Dr. Keele is honorary secretary of the section on the history of medicine of the Royal Society of Medicine of London.

ILLINOIS

Hospital Lecture.—The fourth lecture in the ninth annual North Shore Hospital lecture series on "Emotional Forces in the Family" will be held at the hospital, 225 Sheridan Road, Winnetka, Jan. 7, 8:00 p. m. "The Role of Children in the Family" will be discussed by Dr. Sidney Berman, assistant clinical professor of psychiatry, George Washington School of Medicine, Washington, D. C. The Commission on Education of the American Academy of General Practice has approved these lectures for category II credit. All physicians and allied professional personnel are cordially invited to attend.

Personal.—The Illinois State Medical Society has announced that it has selected Dr. Mark Greer, of Vandalia, as the "Outstanding General Practitioner for 1959" and that a plaque emblematical of the honor will be presented to Dr. Greer at the annual meeting of the society in Chicago next May.—Dr. Arthur G. Baker, Pittsburgh, has been appointed director of Lake County Health Department. Previously Dr. Baker was director of the Allegheny County Health Department, served for two years as deputy director of the Pittsburgh Department of Health, and for five years was chief of the section of local health service in the Michigan Department of Public Health.

Chicago

New Building for Medical Center.—An addition to Chicago's West Side Medical Center has begun and Dr. John J. Sheinin, president of Chicago Medical School, has announced that the 10-story, block long, 110,000-square-foot building will be erected at a cost of 4 million dollars. It will have complete facilities for intensive research in biophysics, behavioral science, infectious disease, allergy arthritis, experimental surgery, experimental medicine, metabolism, endocrinology, biochemistry, hematology, cardiology, and oncology. Completion of this new building, the first of the Chicago Medical School's 10-acre campus of buildings, is scheduled for the fall of 1960. The new campus is being developed to include a College of Physicians and Surgeons, a research hospital, nurses' residence, student quarters, and faculty housing. When the new institute is completed it will provide research facilities for over 400 scientists, doctors, technicians, and postgraduate students. The new building will be air conditioned, with special climate control in the animal quarters, and is being provided with pneumatic tube systems and closed circuit TV. Large seminar rooms and exhibit halls will be on the first floor.

INDIANA

Annual Lecture Series.—The Alpha Tau Chapter of the Phi Delta Epsilon Fraternity will hold its annual lectureship series Jan. 30 in the Indiana University School of Medicine Auditorium, Indianapolis. The guest speaker will be Dr. Thomas Gucker, III, medical supervisor of the Rehabilitation Center of the Orthopaedic Hospital of Los Angeles and associated with the faculty of the University of Southern California. His subject is "Rehabilitation—Points of Emphasis."

MAINE

Laboratory Dedicated to Hospital Pathologist.—The Maine Medical Center honored Maine General Hospital's first pathologist, Mortimer Warren, by dedicating its remodeled and enlarged laboratory in his name. Dr. Warren became the first full-time pathologist at the hospital in 1922 and was still active at the time of his death in 1944. The medical staff in donating money to help remodel the laboratory voted to name it in his honor "for his outstanding service to the hospital, his profession and the people of Maine."

MASSACHUSETTS

Medical History Meeting.—The Benjamin Waterhouse Medical History Society will meet at the Massachusetts Memorial Hospital, Boston, Jan. 5, when Donald H. Fleming, Ph.D., visiting professor of history, Harvard University, and professor of the history of science, Yale University, will speak on "Inoculation Controversy of 1721." Reservation for dinner may be made by calling KE 6-8600. All interested are invited to attend the medical history session.

New Building for Mental Patients.—Medfield State Hospital played host on a tour of the new George O. Clark Reception Building. Built at a cost of $2,250,000, the four-story building is designed for the care of mental patients. The main feature is that it centralizes the admission department, the medical and surgical unit, social service, and continued treatment. The new structure will house 196 patients. This is Medfield State Hospital's first new building since 1914. The Clark Building has two complete operating rooms; a physiotherapy laboratory; ear, nose, and throat, eye and foot clinics; cystoscopic room; pharmacy; x-ray laboratory; and electroshock and insulin treatment suites. The building is named for Dr. George O. Clark, who

served 36 years as trustee and as chairman of Medfield State Hospital's board of trustees from 1939 to 1948.

Anniversary for Psychoanalytic Society.—The 25th anniversary of the founding of the Boston Psychoanalytic Society and Institute was held Nov. 30 in Boston. The creative role played by Boston psychoanalysts in the development in the United States of their specialty was featured in an afternoon and evening program, and the relations of the society and institute to the Harvard Medical School and the Boston University School of Medicine, to mental and general hospitals in the Boston area, to child psychiatry, social work, and to the social sciences generally were discussed.

MICHIGAN

Plans Announced for Research Building.—Construction of a $2,500,000 Research Building which will be owned jointly by University Hospitals and Western Reserve University School of Medicine is tentatively set for next summer. This will be the first major expansion of research facilities in more than 30 years. The building was made possible through grants from the U. S. Public Health Service, the Hanna Fund, and Republic Steel. Containing about 100,000 square feet, it will be used principally by the departments of medicine and preventive medicine. The L-shaped building will extend east from Lakeside Hospital. The entire building will have two floors underground, and the main stem will be three stories high and the wing will be four stories. The Public Health Service grant amounted to $1,253,686 and was equaled by private gifts. Republic Steel contributed $40,000 and the Hanna Fund pledged the balance. A second grant of $376,245 is to be used for the remodeling of the School of Medicine. This includes air conditioning the entire building and modernizing research laboratories of the basic science departments. Dr. Joseph T. Wearn, dean of Western Reserve University School of Medicine, said that funds are needed to match this sum.

Kenny Hospital and Rehabilitation Institute Affiliate.—The Elizabeth Kenny Foundation has moved its in-patient facilities to the recently completed $3,500,000 Rehabilitation Institute of Metropolitan Detroit, 261 Brady Street, adjacent to Harper Hospital, according to a joint announcement by E. J. Rollings, executive vice-president of the foundation's Michigan chapter, and Dr. Joseph N. Schaeffer, director of RIMD. The move climaxes an expanding rehabilitation program which the Kenny Foundation has supported, both nationally and locally, for the past several years. In addition to polio, a growing emphasis has been placed on helping victims of other crippling and degenerative diseases. Rehabilitation of the chronically ill and disabled, which number 57,000 in the Detroit area, will be a unified objective of both RIMD and the Elizabeth Kenny Foundation. Services include Rehabilitation Nursing, Physical Therapy, Occupational Therapy, Speech and Hearing, Activities of Daily Living, Medical Social Services, Vocational Counseling, and Psychological Services. Associated with Wayne State University College of Medicine, RIMD will also serve as a training center for doctors, nurses, therapists, psychologists, social workers, and other rehabilitation personnel. The Elizabeth Kenny Hospital has been located in Farmington since 1953. All in-patients and necessary hospital equipment were transferred to the new quarters of RIMD on September 11. The Kenny Foundation, which is supported by the United Foundation and the Michigan United Fund, will continue to operate its new out-patient facility in Ferndale, Mich.

MINNESOTA

Dr. Magath Honored by Clinical Pathologists.—Dr. Thomas B. Magath, head of the section of clinical pathology of the Mayo Clinic from 1946 to 1958, and professor of pathology in the Mayo Foundation, was honored Nov. 4 in Chicago at a dinner meeting of the American Society of Clinical Pathologists and the College of American Pathologists. Dr. Magath received the Ward Burdick award of the American Society of Clinical Pathologists, described as "a gold medal which shall be presented to that Fellow who, in the opinion of the Research Committee, has presented the most meritorious contributions to the science of clinical pathology." Dr. Magath has served as president of the society, the Minnesota State Board of Health, and the Minnesota Academy of Science.

NEBRASKA

Meeting on Indian Health.—Indian health was discussed when Creighton University medical and dental faculty members met with Indian medical, dental, and pharmacy officers from a six-state area Nov. 13-14. Present were Dr. Joseph H. Gerber, medical officer for the Aberdeen Area, Division of Indian Health, U. S. Public Health Service, and members of the Aberdeen Area Medical, Dental and Pharmacy Officers Association, including Dr. Emery A. Johnson, Winnebago, association president. The Aberdeen area includes Nebraska, North Dakota, South Dakota, Minnesota, Iowa, and Wisconsin. The program featured Benjamin L. Lynch, D.D.S., dean of the Creighton University School of Dentistry; Dr. Benedict R. Walske, professor of surgery, Creighton School of Medicine; Dr. Robert P. Heaney, assistant professor of medicine; Dr. Harold Ladwig, assistant professor of neurology; Dr. Robert J. Luby, instructor in obstetrics and gynecol-

ogy; and Dr. John R. Mitchell, assistant professor of pediatrics. Dr. Richard L. Egen, assistant dean, School of Medicine, spoke at the group's banquet in Sioux City Nov. 13. The two-day continuing education program for health officers was related to the referral system between the Winnebago Indian Hospital, which is diagnostic center for the Aberdeen Area, and Creighton University School of Medicine, Omaha. This system, in conjunction with the United States Public Health Service, helps care for indigent Indians in the area.

NEW YORK

Dr. Duthie Comes to Rochester.—Dr. Robert B. Duthie, of the Institute of Orthopedics, Royal National Orthopedic Hospital, in London, England, has been appointed professor of orthopedic surgery and head of the division at the University of Rochester School of Medicine and Dentistry. Dr. Duthie, who began his new duties on Oct. 1, has had clinical, teaching, and research experience in England, Scotland, and Malaya, where he was on active military service from 1949-51 as a captain in the Royal Army Medical Corps. He received the advanced degree of Master of Surgery with distinction from the University of Edinburgh in 1956, when he was awarded the gold medal for his thesis, "The Histochemistry of the Organic Phase of Postfoetal Osteogenesis." Last year he received the President's Prize of the Societe Internationale de Chirurgie for his experimental work on osteogenesis. Dr. Frederick N. Zuck, associate professor of orthopedic surgery, acting head of the division since the retirement of Dr. Russell P. Schwartz last year, continues as vice-chairman.

New York City

Orchestras for Doctors.—Physicians, dentists, and members of allied professions are invited to become members of two orchestras in New York City. Nonmedical musicians may also join. The Doctors' Orchestral Society of New York rehearses Thursday evenings in the auditorium of the Stuyvesant High School, 15th Street and First Avenue, New York City, at 8:30 p. m. The Brooklyn Doctors' Symphony meets Wednesday evenings in the auditorium of the Brooklyn High School of Home Making at 901 Classon Ave., corner of Washington Avenue, Brooklyn, at the same time. For information write Dr. Benjamin A. Rosenberg, 909 President St., Brooklyn 15: NEvins 8-2370.

Invite Exhibits for Health Exposition.—Manufacturers of drug and medical products, sanitary aids, foods, and other health-related products and services are being invited to participate in the second annual Health Exposition, a health education project of the New York City Department of Health, to be held in the New York Coliseum Aug. 5-15, 1959. The Advisory Council is headed by Morey F. Fields, Ed.D., director of Public Health Education for the New York City Department of Health. An attendance survey at the 1958 show revealed that visitors enjoyed unusual and dramatic exhibits which told an important story. Many of the people interviewed said they would like to see more demonstrations and tests, and more action with either animals or humans participating. For information write the City of New York Department of Health, 125 Worth St., New York 13.

Study of Gastric Cancer.—The New York City Department of Health, five hospitals, and a medical group are conducting a study of gastric cancer involving more than 6,000 persons. The department, hospitals, and group have already examined more than 6,000 selected persons for gastric acidity and found that more than 1,000 of those examined had little or no acid in their gastric juice. Previous studies showed that persons with little or no gastric acidity are three to four times more likely to develop gastric cancer than are persons with normal levels of acidity. The investigators will follow up each of those persons who were found to have little or no gastric acidity to determine whether they will develop cancer. This follow up will take three to five years. The study is being directed by the Bureau of Adult Hygiene of the Department of Health, of which Dr. Abraham Oppenheim is director. Those participating in the investigation are Beth El, Beth Israel, Brooklyn Jewish, Mt. Sinai, and Polyclinic hospitals, the Pack Medical Group, and the New York City Health Department's East Harlem Cancer Prevention-Detection Center. The Pack Medical Group is an organization of private physicians who specialize in cancer.

Dedicate General Hospital.—The new 9-million-dollar Misericordia General Hospital at 600 E. 233rd Street, Bronx, was dedicated Sept. 7, 3:00 p. m. Francis Cardinal Spellman, Mayor Robert F. Wagner, and Bronx Borough President, James J. Lyons, participated in the ceremonies. The new plant will serve the Bronx and lower Westchester. It replaces the original Misericordia Hospital at 531 E. 86th Street, Manhattan, founded by the Sisters of Misericorde 70 years ago. The hospital includes a seven-story general hospital building of 210 beds, a six-story nursing school and residence for 150 nurses, and a three-story shelter for unmarried mothers. On the ground floor of the main building are services facilities. Administrative offices, intern quarters, admitting office, and medical records library occupy the first floor. Outpatient departments, laboratories, and x-ray and emergency departments are located on the second floor. The third floor contains the air-conditioned surgical suite with 74 beds and equipment for all specialized types of surgery. The department of

surgery will have a teaching affiliation with the Bronx Municipal Hospital and the Albert Einstein College of Medicine. The obstetrical suite occupies the south wing and central area of the fourth floor, and the north wing provides 40 beds for gynecological patients. On the fifth floor are 43 patient beds and an 18-bed pediatrics department, together with the department of medicine, research laboratory, and the central sterile supply section for the entire hospital. The sixth and seventh floors contain the chapel and convent. Misericordia Hospital is one of 15 general hospitals of the archdiocese affiliated with the Department of Health and Hospitals of New York Catholic Charities.

NORTH CAROLINA

Fatalities from Fires in 1957.—One-hundred and ninety-seven North Carolinians lost their lives in fires in 1957. Burns and other deaths associated with fire are the second most important cause of accidental death in the home, outranked only by falls. Normally, deaths due to burns in North Carolina as well as nationally occur most frequently among persons 65 years of age and older, but, in the state in 1957 more than 33% of the fatal fire accidents involved children under 15 years of age, and most of these were in the preschool age group.

OREGON

New Trudeau Society.—The Oregon Trudeau Society was organized on May 14 as the medical section of the Oregon Tuberculosis and Health Association. The following officers were elected: president, Dr. William Cohen, Portland; president-elect, Dr. Donald E. Olson, Portland; secretary-treasurer, Dr. Walter A. Noehren, Sandy. This brings the number of state Trudeau societies to 38.

VIRGINIA

Dr. Leavell Named Assistant Dean.—Dr. Byrd S. Leavell was named assistant dean of the University of Virginia School of Medicine, Charlottesville. He will succeed Dr. Henry B. Mulholland, who retired at the age of 65. Dr. Mulholland will continue his medical practice and teaching duties as professor of internal medicine.

GENERAL

Poison Control Centers.—The American Association of Poison Control Centers was formed in Chicago Oct. 21. Officers elected were as follows: president, Dr. Robert J. Grayson, organizer of the poison control center, Jackson Memorial Hospital, University of Miami School of Medicine; vice-president, Dr. William C. Adams, University of Louisville School of Medicine; and secretary-treasurer, Harry W. Raybin, New York City Department of Health. Membership in the organization is open to persons and organizations interested in poison control programs. The group will have as its aims the stimulation of scientific research and education on toxic substances, assistance to state and local officials and to voluntary agencies in the field of poison control, setting up standards for operation of poison control centers, the provision of information to the public, and the development of information services, insurance liability programs in this area, and warning leaflets.

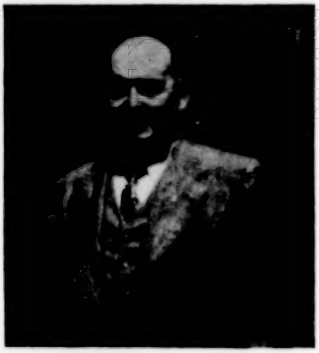
Child Growth.—Today's children are taller and heavier than those of a generation ago, according to statisticians of the Metropolitan Life Insurance Company. Comparison of measurements for Michigan children made recently with those in 1937-1939 shows consistently higher figures for today's children. Among boys under 9, average heights were greater by a fraction of an inch, and at ages 9 and over by an inch or more. Among girls the difference was an inch as early as age 8. The increase in average weight ranged from more than 2 pounds at age 7 to as much as 13 pounds at age 14. According to statisticians, moreover, the ultimate adult height has increased gradually. Evidence for this is available from data on adults in successive age groups, from father-son and mother-daughter comparisons of college entrants, from Selective Service data for the two World Wars, and from comparative figures on conscripts in various European countries.

Three Researchers Win Nobel Prize in Medicine.—The 1958 Nobel Prize in Medicine has been presented to George Wells Beadle, D.Sc., Pasadena, Calif. and Edward Lawrie Tatum, Ph.D., New York City (jointly), and Dr. Joshua Lederberg, Ph.D., Madison, Wis. Half of the $41,250 award was given to Dr. Beadle, of the California Institute of Technology, and Dr. Tatum, of the Rockefeller Institute, who until last year was at Stanford University, San Francisco. The other half of the prize went to Dr. Lederberg, chairman of the department of medical genetics, University of Wisconsin School of Medicine. Next April he will head a new department of genetics at Stanford University School of Medicine. Drs. Beadle and Tatum reportedly established the new field of biochemical genetics. Dr. Lederberg is known for his discovery that certain types of bacteria reproduce by fusing together. In 1946 Drs. Tatum and Lederberg together received acclaim for their discovery of bi-parental inheritance and sexual reproduction in bacteria strains.

Society News.—The officers of the **American Society for the Study of Arteriosclerosis** are as follows: president, Dr. James C. Paterson, London, Ontario, Canada; vice-president, Forrest E. Kendall, Ph.D., Welfare Island, New York City; secretary-treasurer, Dr. Otakar J. Pollak, P. O. Box 228, Dover, Del.—The new officers of the **American Association for**

the Surgery of Trauma are Drs. Truman G. Blocker Jr., Galveston, Texas, president; James K. Stack, Chicago, president-elect; Harrison L. McLaughlin, New York City, vice-president; William T. Fitts Jr., Philadelphia, secretary; Raymond Householder, Chicago, treasurer; and Preston A. Wade, New York City, recorder.——The new slate of officers for the **Western Industrial Medical Association, Inc.,** for 1958-1959 is: president, Dr. Edward J. Zaik, Los Angeles; vice-president, Dr. Verne G. Ghormley, Fresno, Calif.; secretary, Dr. Avon C. Remington, Los Angeles; treasurer, Dr. Clarence L. Lloyd, Los Angeles; assistant secretary, Miss Esther Klingsheim, Los Angeles; and assistant treasurer, Mrs. Olga Wolf, Los Angeles.

Wanted by the FBI.—The Federal Bureau of Investigation requests the cooperation of all physicians in the United States in locating Martin L. Manson, who was indicted by the Federal Grand



Martin L. Manson.

Jury at Los Angeles Feb. 25, 1953, for violation of the National Bankruptcy Act, and who may be under treatment for a tumor. For years Manson operated a tailor shop in Santa Barbara under the firm name of "Martin's." He also established several dry cleaning shops and either abandoned or closed them after a few months, moving to new locations.

Manson, according to the FBI, is white, 69 years old, 5 ft. 7½ in. tall, weighs about 170 lbs., is portly, has light blue eyes, mixed grey and brown hair, thin on top. He lists his occupation as a tailor, and is proud, boastful, and self-assertive. He is married and has a daughter.

Manson is known to have used the following aliases: Martin Luther Manson, Martin Leonard Manson, Bill Billinger, Martin Martinez, Rue Max Adams, Rue Leonard Adams, L. Martin, M. Leonard, Martin Leonard, Leo Leonard.

Any person having information which might assist in locating this fugitive is requested to immediately notify the Director of the Federal Bureau of Investigation, U. S. Department of Justice, Washington 25, D. C., or the Special Agent in Charge of the nearest FBI Division, the telephone number of which is on the first page of local telephone directories.

Award Honors Elizabeth Blackwell.—Mrs. William Larimer Mellon Jr., of Deschapelles, Haiti, received the first Elizabeth Blackwell award of Hobart and William Smith Colleges, Geneva, N. Y., for "outstanding service to mankind." The award was made by the Rev. Dr. Louis M. Hirshson, president of the colleges, at a special convocation to celebrate the 50th anniversary of the founding of William Smith College for women. It is named to commemorate the life and works of Elizabeth Blackwell, reportedly the first woman doctor in the world, who received her M.D. degree from the medical department of Hobart (then Geneva) College in 1849. The award is a simple gold medal, somewhat larger than a silver dollar. Gwen Grant Mellon, with her husband, Dr. William L. Mellon Jr., established the 75-bed Hospital Albert Schweitzer at Deschapelles, Haiti, in 1956 to serve the hundreds of thousands of people in the 600 square miles of the valley of the Artibonite River. Cost of the hospital, in excess of 2 million dollars, and an annual operating deficit in excess of $250,000 are paid for by the Grant Foundation, a Pennsylvania nonprofit corporation established by Dr. Mellon in honor of his wife, whose maiden name was Grant. Additional gifts to the foundation and its work are received from people all over the world, but its principal source of income has been Dr. and Mrs. Mellon.

Psychiatrists Dedicate Office Building.—The dedication of a new central office building in Washington, D. C., for the American Psychiatric Association was held Oct. 31. Secretary of Health, Education and Welfare Arthur S. Flemming gave the dedicatory address. The American Psychiatric Association was founded in 1844 by 13 physicians under the title Association of Medical Superintendents of American Institutions for the Insane. In 1892, by which time it had about 250 members, the name was changed to the American Medico-Psychological Association. In 1921, when it had 1,000 members, it assumed its present title. By 1950 the association's membership had grown to 6,000; this year it passed the 10,000 mark. The new $300,000 headquarters is a converted town house, owned outrightly by the American Psychiatric Association and made possible by voluntary contributions from its members. It houses a staff of 35. The association provides a wide range of information and consultation services

to state governments on mental health and hospital problems; it inspects, rates, and sets standards for mental hospitals; it publishes the *American Journal of Psychiatry*, the magazine, *Mental Hospitals*, and other professional books, reports, and proceedings; it issues the official Nomenclature for Mental Disorders; it administrates special research and conference projects; it furnished information to the public about psychiatry. It is a nonprofit association. The medical director, Dr. Mathew Ross, is the senior staff employee of the association. He took office in September this year, succeeding Dr. Daniel Blain.

CORRECTION

Licensed Foreign-Trained Physicians.—Table 29 entitled "Foreign-Trained Physicians Licensed by State Boards, 1952-1957," published in the State Board Number of THE JOURNAL, May 31, 1958, page 622, reported incorrect figures for the year 1956. The total for the fifth column entitled "Examination" for the year 1956 should have been 1,012. This likewise changes the total column in this section to 5,786 and the grand total to 6,738. The figures given for each state are incorrect and anyone referring to this table should consult the Council on Medical Education and Hospitals for the correct figures for each state.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application is Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application is Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I.* Various parts of the United States and Canada, January 16. Candidates notified of their eligibility to participate in Part I must submit their case abstracts within thirty days of notification of eligibility. No candidate may take the written examination unless the case abstracts have been received in the office of the Secretary. *Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written,* qualifying test (Part I), Various Cities, Jan. 26. *Oral.* Philadelphia, June 2; St. Louis, Oct. 6-10. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

AMERICAN BOARD OF UROLOGY: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Andes, T. Eugene, Gardner, Mass.; Temple University School of Medicine, Philadelphia, 1940; member of the Massachusetts Medical Society and the American Psychiatric Association; certified by the National Board of Medical Examiners; veteran of World War II; served on staffs of hospitals in Harrisburg, Pa., Martinsburg, W. Va., Morganton, N. C., and Lakeland, Ky.; served as assistant superintendent of Gardner (Mass.) State Hospital; died in the Temple University Hospital, Philadelphia, Oct. 10, aged 44, of pulmonary emphysema.

Aszuk, Joseph Charles Ⓜ Wilkes-Barre, Pa.; Temple University School of Medicine, Philadelphia, 1926; veteran of World War I; from 1928 to 1951 on the staff of Mercy Hospital and since 1951 on the staff of the Veterans Administration Hospital, where he died Oct. 18, aged 62, of carcinoma of the bladder.

Bachmann, George William, Smith River, Calif.; University of Buffalo School of Medicine, 1906; veteran of the Spanish-American War; died Sept. 20, aged 79, of a heart attack.

Bernard, Louis Emile Ⓜ Croton-on-Hudson, N. Y.; born in 1898; University of Montreal Faculty of Medicine, Montreal, Que., Canada, 1925; Long Island College Hospital, Brooklyn, 1931; fellow of the American Psychiatric Association; served an internship at the Kings Park (N. Y.) State Hospital and a residency at the Rockland State Hospital in Orangeburg; member of the Association for the Advancement of Psychotherapy, New York Society for Clinical Psychiatry, the Bronx Society of Neurology and Psychiatry, the Westchester Academy of Medicine, and New Jersey Neuropsychiatric Society; served on the staff of the Croton Manor Sanitarium; owner and director of the Stony Lodge in Ossining; consulting psychiatrist at Phelps Memorial Hospital in North Tarrytown, where he died Oct. 23, aged 60.

Beyer, John Andrew II Ⓜ Madison, Wis.; born in Dover, N. J., March 11, 1921; Columbia University College of Physicians and Surgeons, New York City, 1945; interned at the New York Post-Graduate Medical School in New York City and served a fellowship in internal medicine at the New York Hospital; certified by the National Board of Medical Examiners and the American Board of Internal Medicine; instructor of pharmacology at his alma mater from 1946 to 1948; an associate of the American College of Physicians; member of the American Federation for Clinical Research and the Wisconsin Heart Association; member of the Kiddie Camp Convalescent Home for Rheumatic Heart Disease; member of the mobile clinics, Wisconsin Heart Association; member of the board and house physician, Oakwood Lutheran Home; consulting cardiologist, Visiting Nurse Service; member of the staff and chairman of the records committee, Madison General Hospital; director, rheumatic fever clinic, St. Mary's Hospital; chief, cardiovascular section, and captain, U. S. Army Medical Corps, Percy Jones Army Hospital, Battle Creek, Mich., from 1951 to 1953; died in Sioux Falls, S. D., Oct. 18, aged 37, of injuries received in an automobile accident.

Blaine, Edward Smith Ⓜ Los Angeles; Milwaukee Medical College, 1911; served on the faculty of Marquette University School of Medicine in Milwaukee, Northwestern University Medical School in Chicago, and the College of Medical Evangelists in Loma Linda and Los Angeles; specialist certified by the American Board of Radiology; veteran of World War I; died at his home in San Marino, Calif., Oct. 8, aged 75.

Bocricke, Oscar Eugene, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1898; an associate member of the American Medical Association; served on the faculty of his alma mater; died Oct. 16, aged 86.

Brown, Joseph Nichols, Campti, La.; Hospital College of Medicine, Louisville, Ky., 1906; member of the Louisiana State Medical Society; past-president of the Natchitoches Parish Medical Association; died in Shreveport Oct. 10, aged 81.

Burch, Newnan Burgess, Hot Springs National Park, Ark.; University of Tennessee College of Medicine, Memphis, 1917; for many years associated with the Wade Clinic; owner of the Burch Clinic; died in the Ochsner Foundation Clinic in New Orleans, Oct. 18, aged 71.

Burke, Joseph Peter, Scranton, Pa.; Georgetown University School of Medicine, Washington, D. C., 1913; veteran of World War I; on the staffs of State, Mercy, and St. Mary's hospitals; died in the Veterans Administration Hospital in Wilkes-Barre Oct. 18, aged 75, of asthma.

Burleson, William Brown Ⓜ Plumtree, N. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; died Oct. 2, aged 76.

Ⓜ Indicates Member of the American Medical Association.

Butler, Harry M., Hutchinson, Kan.; Ensworth Medical College, St. Joseph, Mo., 1905; served on the staffs of the Hadley Memorial and St. Anthony's hospitals in Hays; died in the Grace Hospital Oct. 10, aged 81, of pneumonia.

Carman, John Thomas, Franklin, Ky.; University of Tennessee Medical Department, Nashville, 1898; an associate member of the American Medical Association; died in the Carter Moore Hospital Oct. 1, aged 88, of heart disease and a fractured hip as the result of a fall.

Charles, Thomas Goodell Ⓜ Beardstown, Ill.; Northwestern University Medical School, Chicago, 1909; chairman of the Beardstown Board of Health; veteran of World War I; died in St. Luke's Hospital, St. Louis, Oct. 10, aged 71.

Chenoweth, Laurence Benjamin Ⓜ Cincinnati; Johns Hopkins University School of Medicine, Baltimore, 1919; served on the faculty of the Cornell University in Ithaca, N. Y., and as director of the department of hygiene and student health service, University of Cincinnati; past-president of the American College Health Association; for three years president of the Phi Epsilon Kappa; joint author of "School Problems," "Personal Hygiene," and other books on hygiene and health; died Oct. 17, aged 67, of coronary occlusion and arteriosclerotic heart disease.

Close, John Harry Ⓜ Minersville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1935; interned at the Harrisburg (Pa.) Hospital; died in the A. C. Milliken Hospital in Pottsville Sept. 24, aged 51, of hypertensive heart disease.

Coffee, John Young Jr. Ⓜ Huntsville, Ala.; Medical College of Georgia, Augusta, 1947; served in the Korean War and World War II; interned at Jefferson–Hillman University Hospital in Birmingham; formerly resident in pediatrics at the Employees Hospital of the Tennessee Coal, Iron and Railroad Company in Fairfield; served as vice-president of the Madison County Medical Society; died in the Brookhaven National Laboratories in Upton, L. I., Oct. 5, aged 36, of brain tumor.

Council, Melton Downie, Vero Beach, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1911; an associate member of the American Medical Association; veteran of World War I; died in the Veterans Administration Hospital, Richmond, Va., Oct. 5, aged 74.

Creighton, Matthew Eugene Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1925; fellow of the International College of Surgeons; served on the faculty of his alma mater; member and past-president of the medical staff, St. Bernard Hospital; died Oct. 21, aged 59, of coronary occlusion.

Cronin, Herbert Joseph, Cambridge, Mass.; Harvard Medical School, Boston, 1911; member of the Massachusetts Medical Society; died in Boston Oct. 3, aged 69, of bronchopneumonia.

Daniel, Samuel Greene Ⓜ Marshall, Ark.; University of Louisville (Ky.) School of Medicine, 1895; died Oct. 1, aged 90.

Danskin, Melville George, Billings, Mont.; born in Colo, Iowa, Oct. 9, 1883; Northwestern University Medical School, Chicago, 1909; an associate member of the American Medical Association; a past-vice-president of the Montana Medical Association; for many years practiced in Glendive and eastern Montana; appointed county health officer for Dawson County in 1916, serving in this capacity for many years; from 1923 to 1927 mayor of Glendive and served as president of the state public health association and as the first president of the local Kiwanis Club; in 1916 named physician in charge of the Dawson County Hospital, holding that post for many years; died Oct. 11, aged 74.

Davis, James Matheson Ⓜ Wadesboro, N. C.; Columbia University College of Physicians and Surgeons, New York City, 1913; veteran of World War I; on the staff of the Anson County Hospital; died in Denton, Oct. 12, aged 69, of acute coronary occlusion.

Delbaum, Harry, Brooklyn; Long Island College Hospital, Brooklyn, 1935; member of the Medical Society of the State of New York; on the staff of the Unity Hospital; died Oct. 12, aged 49, of coronary disease.

Di Rienzo, George Michael Ⓜ Napa, Calif.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1948; member of the American Academy of General Practice; captain, U. S. Air Force from July 1, 1949, to Sept. 3, 1951; on the staff of the Queen of the Valley Hospital; died Oct. 14, aged 32, of coronary arteriosclerosis.

Dudley, Augustus William Ⓜ Cambridge, Mass.; Harvard Medical School, Boston, 1895; veteran of World War I; fellow of the American College of Surgeons; for many years on the staff of the Mount Auburn Hospital; died in the Westboro (Mass.) State Hospital Oct. 7, aged 90, of carcinoma of the colon.

Dunn, James Ⓜ Davenport, Iowa; Rush Medical College, Chicago, 1904; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; honorary life member and secretary of the Iowa and Illinois Central District Medical Society, and served as editor of its bulletin; at one time a medical officer in the U. S. Public Health Service; on the staffs of Mercy and St. Luke's hospitals; died in Muscatine Oct. 11, aged 79.

Dusthimer, Oren Isaiah ⊗ Zanesville, Ohio; Ohio Medical University, Columbus, 1906; honored in June, 1956, when the Muskingum County Academy of Medicine presented him with a 50-year pin; received a certificate of distinction from the Ohio State Medical Association; on the staffs of the Good Samaritan Hospital and the Bethesda Hospital, where he died Oct. 13, aged 82, of rheumatic heart disease and pneumonia.

Ebeling, William Bruno, Brooklyn; Columbia University College of Physicians and Surgeons, New York City, 1914; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; on the staff of the Brooklyn Eye and Ear Hospital; died in the General Hospital of Monroe County, East Stroudsburg, Sept. 13, aged 67, of mesenteric thrombosis.

Farrar, William Charles, Birmingham, Ala.; Birmingham Medical College, 1908; died Oct. 11, aged 79, of uremia and cardiovascular disease.

Field, Thomas Sullivan ⊗ Green Cove Springs, Fla.; Dartmouth Medical School, Hanover, N. H., 1910; fellow of the American College of Surgeons; veteran of World War I; on the staffs of Duval County Medical Center, St. Luke's Hospital, and St. Vincent's Hospital in Jacksonville, where he died Oct. 10, aged 72, of bronchiectasis.

Fitzporter, Alonzo Leo ⊗ Muskogee, Okla.; St. Louis University School of Medicine, 1910; service member of the American Medical Association; retired from the Veterans Administration regional office, in 1954; served most of his career in various veterans hospitals throughout the country; veteran of World Wars I and II; died in Tucson, Ariz., Oct. 13, aged 74, of coronary occlusion.

Frey, Robert David, Allentown, Pa.; Jefferson Medical College of Philadelphia, 1890; died in the Allentown Hospital Oct. 10, aged 90, of uremia and generalized arteriosclerosis.

Friedman, Joseph ⊗ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1931; member of the American Academy of General Practice; veteran of World War II; died Oct. 4, aged 56.

Frymire, Ewett Waverly ⊗ Frankfort, Ky.; University of Louisville Medical Department, 1905; died in the Norton Memorial Infirmary Oct. 9, aged 77, of arteriosclerotic heart disease.

Gallagher, James Francis ⊗ Freeland, Pa.; Temple University School of Medicine, Philadelphia, 1925; on the staffs of the Hazleton State and St. Joseph's hospitals; member of the board of directors of the Hazleton Heart Association; died Oct. 7, aged 58, of coronary disease.

Gallivan, Thomas Humphrey ⊗ Santa Ana, Calif.; Yale University School of Medicine, New Haven, Conn., 1909; specialist certified by the American Board of Otolaryngology; served on the staffs of St. Francis Hospital in Hartford, Conn., Community and Doctors hospitals in Santa Ana, and St. Joseph Hospital in Orange, where he died Oct. 14, aged 73.

Gibbons, Charles Kimball, Kearney, Neb.; Northwestern University Medical School, Chicago, 1902; past-president of the Buffalo County Medical Society; veteran of World War I; on the staff of the Good Samaritan Hospital; member of the Chamber of Commerce and the Rotary Club; died Oct. 3, aged 81, of gastrointestinal bleeding and shock.

Gleason, Ralph Sidney, Deer Island, Maine; Tufts College Medical School, Boston, 1929; interned at Eastern Maine General Hospital, Bangor; member of the Massachusetts Medical Society; for many years practiced in Wellesley Hills, Mass.; served on the staff of the Newton-Wellesley Hospital in Newton, Mass.; veteran of World War II; died Oct. 13, aged 53, of pulmonary hemorrhage.

Goudelock, John Jefferies, Monroe, N. C.; Medical College of South Carolina, Charleston, 1923; member of the Medical Society of the State of North Carolina; associated with the Ellen Fitzgerald Annex of the Union Memorial Hospital; was found dead in bed Oct. 13, aged 58, of a heart attack.

Grant, William Lee ⊗ St. Paul, Minn.; Marquette University School of Medicine, Milwaukee, 1955; service member of the American Medical Association; interned at the Illinois Central Hospital in Chicago; served as a captain in the U. S. Army Reserve and as head of the outpatient clinic at Fort Leonard Wood, Mo.; died Oct. 18, aged 29, of coronary occlusion.

Gray, Robert Hollingsworth, Shreveport, La.; Bellevue Hospital Medical College, New York City, 1895; for many years on the staff of the Schumpert Sanitarium, where he died Oct. 5, aged 87, of injuries received when struck by an automobile on Sept. 27.

Hargrove, Henry C., Beckley, W. Va.; Howard University College of Medicine, Washington, D. C., 1908; died Oct. 1, aged 78.

Henry, John Robert, Winston-Salem, N. C.; Leonard Medical School, Raleigh, 1908; medical director of the Winston Mutual Life Insurance Company, a post he held for 39 years; medical director of Safe Bus Company; attending physician at the Kate Bitting Reynolds Memorial Hospital, where he died Oct. 3, aged 74, of gastrointestinal hemorrhage from esophageal varices, and cirrhosis of the liver.

Herbert, William, Dunedin, Fla.; Long Island College Hospital, Brooklyn, 1909; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; formerly practiced in Brooklyn, where he was associated with the Brooklyn, Bushwick, and Brooklyn Eye and Ear hospitals; died in the Mease Hospital Sept. 26, aged 76, of arteriosclerotic heart disease.

MacBride–Dexter, Edith ® Sharon, Pa.; born in Grove City, Pa., May 3, 1887; Woman's Medical College of Pennsylvania, Philadelphia, 1910; from 1912 to 1917 physician for girls, Grove City (Pa.) College; appointed secretary of health, Commonwealth of Pennsylvania in 1935, serving until 1939; on Aug. 12, 1938, was awarded Pennsylvania's "meritorious service medal" by the governor, for distinguished service in public health during widespread floods of 1936, and for a progressive program as secretary of health; past-vice-president of the Medical Society of the State of Pennsylvania; for ten years secretary of the Mercer County Medical Society; served as chairman of the advisory board of health, as member of the sanitary water board, state board of medical education and licensure, state dental council and examining board, and state board of undertakers, Commonwealth of Pennsylvania; member of the Pennsylvania Public Health Association and served as chairman of executive committee; from 1935 to 1939 member of the Conference of State and Territorial Health Authorities; member of the Conference of State and Provincial Health Authorities of North America and the Pan American Association of Ophthalmology; at various times vice-chairman, secretary, and chairman of the Secretaries Conferences of Component County Medical Society of the State of Pennsylvania; from 1919 to 1935 on the staff of the C. H. Buhl Hospital, now known as the Sharon General Hospital, where she returned to the staff in 1939; ophthalmologist to the Sharon Plant, Westinghouse Electric Manufacturing Company and National Malleable and Steel Castings Company; died Oct. 11, aged 71, of a heart attack.

McKenna, Henry Joseph ® Louisville, Ky.; born in Louisville March 30, 1885; University of Louisville School of Medicine, 1910; associated with Mayo Clinic in Rochester, Minn., from July 1, 1912, to Feb. 1, 1915; veteran of World War I; formerly practiced in Kansas City, Mo., where he was president of the staff of St. Mary's Hospital; at one time president of the McKenna Distillery of Fairfield; fellow of the American College of Surgeons; member of the Industrial Medical Association; served on the staff of St. Joseph Hospital and as medical director of the Bendix Products Division of the Bendix Aviation Corporation in South Bend, Ind.; died in St. Joseph Infirmary Oct. 8, aged 73, of peritonitis and pneumonia.

Mateer, Harry Oliver ® Pittsburgh; Pulte Medical College, Homeopathic, Cincinnati, 1910; Hahnemann Medical College and Hospital of Philadelphia, 1912; for many years associated with the health service of the city schools; veteran of World War I; past-president of the Hahnemann Alumni Association; member of the staff of the Shadyside Hospital, where he died Oct. 1, aged 72.

Mendelsohn, Sidney Norman ® Cincinnati; University of Louisville (Ky.) School of Medicine, 1929; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; on the staffs of Our Lady of Mercy Hospital and the Jewish Hospital and Medical Center of Cincinnati, where he died Oct. 4, aged 53.

Meriwether, Ellyson Gwynne ® Memphis, Tenn.; Memphis Hospital Medical College, 1909; member of the American Psychiatric Association; died Oct. 7, aged 73, of cerebral thrombosis and arteriosclerosis.

Metheny, Samuel, Lincoln, Neb.; Lincoln Medical College of Cotner University, 1902; served on the faculty of his alma mater; died in the Bryan Memorial Hospital Oct. 2, aged 94, of intestinal obstruction and coronary thrombosis.

Noyes, John Russell ® Brockton, Mass.; Boston University School of Medicine, 1904; fellow of the American College of Surgeons; for many years associated with the Brockton Hospital, where he served as chief of the eye, ear, nose and throat service; consultant, Jordan Hospital, Plymouth; died Oct. 8, aged 82, of cerebral thrombosis.

Nussbaum, Oscar, New York City; Julius–Maximilians–Universität Medizinische Fakultät, Wurzburg, Bavaria, Germany, 1908; an associate member of the American Medical Association; died in the Jewish Memorial Hospital Oct. 11, aged 78, of intestinal neoplasm.

Rauch, Harvey Milton, Ormond Beach, Fla.; College of Physicians and Surgeons, Baltimore, 1904; member of the staff of St. Joseph's Hospital and the Falk Clinic in Pittsburgh, where he practiced for many years; died Oct. 1, aged 82, of a heart attack.

Reed, Russel Soule ® Seattle; Bennett Medical College, Chicago, 1913; died in the Virginia Mason Hospital Oct. 4, aged 70, of myocardial infarction.

Thorndike, W. T. Sherman, Philadelphia; born in Boston Jan. 16, 1893; Harvard Medical School, Boston, 1920; for many years on the faculty of his alma mater; an associate member of the American

Medical Association; member of the Massachusetts Medical Society; past-president and secretary of the Philadelphia Hospital Association and a member of its executive committee; member of the council on administrative practice, Hospital Association of Pennsylvania, advisory committee to the Commission on Blood Banks, Medical Society of the State of Pennsylvania, and on the advisory board of the Hospital Council of Philadelphia; during World War II served as registrar of the Sixth General Army Hospital in Casablanca and Rome; later served as commanding officer of the 154th Station Hospital in Italy and was discharged in 1946 with the rank of lieutenant colonel; interned at the Boston Lying-In Hospital and the Massachusetts General Hospital in Boston, where he was assistant director for many years; managing director of the Germantown Dispensary and Hospital, where he died Oct. 10, aged 65, of cancer of the prostate with metastasis.

Tillman, Isidor R., Brooklyn; University of Buffalo School of Medicine, 1901; an associate member of the American Medical Association; died Sept. 15, aged 87, of pneumonia, cardiac decompensation, cerebral thrombosis, and generalized arteriosclerosis.

Truex, Barbara Mae Binkley ⊗ Jackson, Tenn.; Vanderbilt University School of Medicine, Nashville, 1942; served an internship at the Barnes Hospital in St. Louis and a residency at the Children's and Cincinnati General hospitals in Cincinnati, Ohio; on the staff of the Jackson-Madison County General Hospital; died Sept. 23, aged 40, of a basal skull fracture as the result of a fall from a horse.

Virden, Charles Edgar ⊗ Kansas City, Mo.; born in Kansas City April 12, 1895; Northwestern University Medical School, Chicago, 1920; assistant clinical professor of radiology at the University of Kansas School of Medicine in Kansas City, Kans.; specialist certified by the American Board of Radiology, Inc.; past-president of the Jackson County Medical Society which in 1947 awarded him its certificate of merit; past-president of the Missouri division of the American Cancer Society and received a gold medal from the American Cancer Society for his work in connection with the disease; past-president of the American College of Radiology, Missouri State Medical Association, Kansas City Southwest Clinical Society, and the Radiological Society of North America; member of the Kansas City Academy of Medicine and the Industrial Medical Association; fellow of the American Geriatrics Society and the American Association for the Advancement of Science; consultant radiologist for the U. S. Public Health Service and the Parsons Tumor Clinic in Parsons, Kan.; instrumental in establishing the cancer clinic at the Kansas City General Hospital; chief radiologist at St. Joseph Hospital, where he served an internship and where he was associated for many years; died in the Georgetown University Hospital in Washington, D. C., Oct. 3, aged 63, of coronary thrombosis.

Whitely, Seals Leftwich ⊗ Durant, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1949; member of the American Academy of General Practice; secretary-treasurer, Atoka, Bryan, Coal Counties Medical Society; served as county superintendent of public health; associated with Durant Hospital; died Sept. 26, aged 37, of teratoma of the mediastinum.

Willmarth, Edwin Hamilton ⊗ New Castle, Pa.; University of Nebraska College of Medicine, Omaha, 1928; on the staffs of the Jameson Memorial Hospital and New Castle Hospital, where he died Sept. 19, aged 57, of cerebral hemorrhage.

Wilson, Eva McClenahan ⊗ Mill Valley, Calif.; Northwestern University Woman's Medical School, Chicago, 1894; member of the Illinois State Medical Society; died Sept. 25, aged 88.

Wooden, James Leonidas ⊗ Clatskanie, Ore.; University of Oregon Medical School, Portland, 1906; veteran of World War I; served several terms on the school board; the citizens of the Clatskanie area honored him with a "Doctor Wooden Day" in August of last year, commemorating 50 years of practice in the community; a fountain in the city park was erected and dedicated in his honor; for many years director of the First National Bank; died in the Emanuel Hospital, Portland, Oct. 7, aged 76, of cancer of the cecum and chest with metastasis and bronchopneumonia.

Zimmerman, Frank Dieffenbach, Schaefferstown, Pa.; Jefferson Medical College of Philadelphia, 1907; an associate member of the American Medical Association; past-president of the Lebanon County Medical Society; president of the Heidelberg Water Company; for many years served as president of the Schaefferstown National Bank, prior to its becoming a branch of the Lebanon Valley National Bank, of which he was director; a charter member of the local Lions Club; on the staff of the Good Samaritan Hospital in Lebanon; died Sept. 27, aged 80, of acute coronary occlusion.

FOREIGN LETTERS

BELGIUM

Lung Cancer.—Prof. J. Firket (*Proceedings of the Royal Society of Medicine of London*) studied air pollution in Liege, an industrial center. He found that the homes of 500 patients with pulmonary cancer were largely concentrated in the center of the city. Many workers were employed in the huge metallurgic establishments just upstream of the city and lived in houses built 10 to 15 years ago. Because of the prevailing wind, the area they all occupied was one of the least polluted by chemical dust, yet the number of workers with pulmonary cancers was fairly large. In contrast, in the center of the area which is surrounded by a horseshoe bend of the Meuse River, immediately northeast of the first area, there were few patients with cancer even though this is a sort of tableland on which dust settles in abundance. There was no industry on the plateau and it has been a pleasant residential area for about 45 years with many trees and occupied by the upper middle class. The extensive dust pollution of this area was not known at the time it was built.

The author was struck by the large number of persons with cancer living in the center of the city and especially in streets beside railways or canals. The attention was drawn to these by their names, "Rue de la gare, Rue de la station, Rue du chemin de fer, and Rue du vicinal." Railway engines were an obvious source of air pollution and steamboats also definitely polluted the air around the docks. In 1955 the incidence of lung cancer in Canada was found to be five times higher among locomotive engineers than among the whole population. Engineers inhaled carcinogenic hydrocarbons either from the sooty exhaust of diesel engines or the smoke of coal-burning locomotives.

In Belgium, too, one can see a striking correspondence between smoke and lung cancer. In the vicinity of factories in Herstal, one can find many men out of work because of cancer, but as the valley runs north the incidence suddenly drops and, at the same time, the smoke disappears. Toward the east the smoke continues and with it the cancer. From five years of research it must be concluded that lung cancer has a complex etiology. Of several factors cigarette smoking is an important, but not an essential, one. Polluted air, and particularly the hydrocarbons contained in soot, appear to be even more important.

The items in these letters are contributed by regular correspondents in the various foreign countries.

BRAZIL

Tetanus Neonatorum.—Dr. Francisco La Scala (*Jornal de pediatria*, vol. 23, September, 1958) reported a series of 56 patients with tetanus neonatorum. He called attention to the low incidence of this disease among Negroes, indicating a racial resistance. Only six of these children recovered despite the use of antitetanic serum and antibiotics. The author advocated as a preventive measure against this complication the immunization of expectant mothers who cannot have the assistance of an aseptic delivery.

Schistosomiasis.—Dr. Luis Rey (*Hospital*, vol. 54, October, 1958) reported that a new focus of schistosomiasis has been discovered within the city of São Paulo. He believed that new foci appear only as a consequence of favorable conditions recently created. Due to the inefficiency of molluscocides and the limitations of chemotherapy, greater emphasis must be placed on sanitary methods of control aimed not against schistosomiasis alone but against all endemic diseases spread through feces and polluted water.

Prevention of Abortion.—Cerruti and Fernandes (*Revista d'obstetricia e ginecologia*, vol. 103, July, 1958) have simplified the technique of interpreting the vaginal smears considering only the eosinophilic index and the progestational modifications. They studied a series of 239 women in the first trimester of pregnancy with threatened abortion, taking one, two, or three smears from each. In 118 patients with a "good prognosis" they had 11% of error with one smear and 6.8% and 5.1% with two and three smears respectively. In 121 patients with a "bad prognosis" the error was 6.6% with one smear and 4.2% with two or three smears. The authors reached the following conclusions. The vaginal smear was of no value as a diagnostic test of pregnancy. In patients with a bad prognosis showing cells indicative of fetal death, this conclusion was invariably correct. The lessening of absence of progestational modifications had a greater prognostic value than the rise of the eosinophilic index. Vaginal smears did not permit differentiation between the phase of ovum death and that of its expulsion. Intensive estrogenic treatment did not alter the appearance of the vaginal smear in pregnancy. An unfavorable vaginal smear found in patients without any clinical signs of abortion had no prognostic value because in such patients pregnancy often proceeded normally.

Statistical study of this material indicated that the progestational modifications had greater value than the eosinophilic index and the examination of a second smear lessened the chances of error and established that within a reasonable range of error it is possible to give a prognosis regarding a threatened abortion. Incipient miscarriage would appear to be due primarily to fetal rather than maternal factors. From a purely clinical point of view it is possible to establish the prognosis of an abortion only when the symptoms and signs become evident. It is then often too late to apply effective preventive measures. The authors found that the pregnandiol level had scant value for the prognosis of threatened abortion because (1) of the relatively low amount of this hormone at the beginning of pregnancy, with little difference between its level at that time and during the secretory phase of menstruation; (2) frequent discrepancy between the expected pregnandiol level and the course of pregnancy; and (3) the great technical difficulty of determining the level. The frog test is easier to make. The repetition of this test is of value for the prognosis of threatened abortion. The vaginal smear is an easy process which can be repeated as required if abortion threatens. Vaginal cytology does not indicate the amount of hormones in the blood but gives a sufficiently accurate idea of the balance between estrogen and progesterone, thus giving advance warning of a hormonal imbalance in patients with threatened abortion.

Polyposis of the Colon.—Dr. Silvio Levy, (*Arquivos de cirurgia clinica e experimental*, vol. 21, 1958) in a series of 67 patients with polyposis of the colon, found carcinoma in 18. One of the most important aspects of this series was the presence of malignant polyps in the first decade of life (25% of the cases). The incidence of polyps in about 6,000 patients was 1.5%. In the diagnosis of the polyp it is important to recognize the lesion, even in asymptomatic patients. X-ray examinations are indispensable for the detection of polyps above the reach of the sigmoidoscope. This higher localization of polyps occurs more frequently than was recognized before the use of the barium enema. The biopsy may be total or partial. The total biopsy represents a complete therapeutic procedure in itself in patients with noninvasive carcinoma. Partial biopsy should never be done if the lesion is small, but it is advisable for polyps measuring more than 1 cm. in diameter, especially if they are sessile or if they present macroscopic signs of malignancy. The operative indications and the choice of the surgical procedure should be based on (1) localization of the polyp, (2) macroscopic appearance of the polyp, (3) microscopic appearance of the previous biopsy specimen, (4) number of polyps and presence of other lesions, (5) age of the patient, and (6) medicosocial factors such as facilities for an efficient follow-up.

The simple excision of the adenoma through an endoscope is indicated for small polyps if the histological appearance does not suggest the presence of malignancy, or for a polyp with a previous biopsy specimen indicating noninvasive carcinoma, grade 1, or carcinoma "in situ." Radical surgical resection is advisable for an invasive carcinoma diagnosed by a previous biopsy or diagnosed after the excision of the lesions, or if the patient cannot be rigorously followed up. For villous adenomas, resection is also preferable. Polyps of the various segments of the colon, which cannot be treated endoscopically, must be explored by laparotomy. It is advantageous always to perform a complete proctoscopy to decide the extent of the resection. If there is suspicion of the presence of metastases, the examination of fragments of regional lymph nodes is of value. Resection is preferable to the simple excision of the polyps and is a much more complete operation. For sessile adenomas a primary segmental resection is imperative. Villous adenomas should be resected with the segment.

INDIA

Plasma Amino Acids in Malignancy.—G. Y. N. Iyer (*Indian Journal of Medical Research*, vol. 46, July, 1958) studied 42 patients with malignancy to determine the levels of free alanine, glutamine, glutamic acid, glycine, serine, tyrosine, valine, leucine, and isoleucine in the plasma; 18 of the patients were suffering from leukemia, 6 had carcinoma of the stomach, 6 had carcinoma of cheek, 4 had cancer of the uterus, 3 had Hodgkin's disease, 2 had cancer of the palate, 2 had cancer of the penis, and 1 had carcinoma of the prostate. Paper chromatography was used for estimation of the amino acids in the plasma. A rise in the glutamic acid level was seen in all patients. The levels of all the other amino acids except glycine showed a fall, and the level of glycine was not significantly changed except that it was raised in all patients with leukemia. No correlation was observed between the type and location of malignancy and the changes in plasma amino acids.

Plasma Insulin Estimation.—Aiman and Kulkarni (*Indian Journal of Physiology and Pharmacology*, vol. 2, July, 1958) stated that because certain diabetics prove resistant to insulin, insulin deficiency may not be the only cause of diabetes. They estimated the plasma insulin level in 5 nondiabetic and 10 diabetic persons by the rat diaphragm method. Insulin therapy was discontinued for 48 hours and carbutamide therapy for 15 days before the assay of plasma insulin. The postprandial blood sugar level was estimated in each case to exclude any latent derangement of carbohydrate metabolism.

The plasma insulin levels in the nondiabetics ranged from 0.7 to 6.3 milliunits per milliliter. In two diabetics who were middle-aged, whose disease had been discovered within a period of less than six months and who did not require insulin, the plasma insulin levels were within the normal range. Four middle-aged diabetics required insulin and responded well to carbutamide or tolbutamide and showed plasma insulin levels that were lower than normal, but these readings were a little higher than those obtained in two other middle-aged diabetics, one of whom did not respond to carbutamide. The remaining two diabetics who were in a younger age group also showed low plasma insulin levels and an evidence of the presence of an excess of anti-insulin factors in their plasma. Thus juvenile diabetes is probably due to an excess of anti-insulin factors circulating in the plasma, while the diabetes of middle age is more probably due to a deficiency of insulin in the plasma. This method can also be used in selecting patients for carbutamide therapy. In the present series, patients with a moderate concentration of insulin in the plasma showed a good response to this therapy, while those with a negligible insulin content failed to respond.

Cesarean Section.—S. Apteka analyzed a series of 1,344 cesarean sections performed at the Cama and Albless Hospitals, Bombay, from 1930 to 1956 (*Journal of the Association of Medical Women in India*, vol. 46, May, 1958). This series represented 1.4% of all deliveries at these hospitals. All cases of ruptured uterus were excluded from these statistics. The incidence was highest in 1940 and 1942 and lowest in 1951, 1952, and 1953. Contracted pelvis accounted for 73.6% of cesarean sections at these hospitals. Most of the patients who come to these hospitals are poor and undernourished and therefore likely to be underdeveloped and to suffer from rickets and osteomalacia. The incidence of repeated cesarean sections was very low—0.6%. This operation was repeated only in patients in whom it was suspected that the scar of the previous operation might give way. All patients who had a cesarean section at one delivery for an indication which was not present at a subsequent pregnancy were allowed to deliver per vaginum under careful observation. The maternal complications for which cesarean section was performed were eclampsia, essential hypertension, intracranial tumor, infective jaundice, and obstructive cholecystitis. The number of cesarean sections performed for osteomalacic pelvis decreased from 53.5% in the years 1930-1934 to 19.6% in the years 1950-1956. This might be due to improved general living conditions.

Other varieties of contracted pelvis did not show any appreciable difference in their incidence. Placenta previa as an indication for cesarean section was seen to be increasing. During the period 1930-1934, of a total of 170 sections, only 1 was performed for this condition, while during the period 1950-1956, 51 of a total of 418 sections were performed for placenta previa. The classic type of operation was performed on 513 patients (38.2%), lower segment operation on 824 (61.2%), cesarean hysterectomy on 6 (0.5%), and extraperitoneal cesarean section on 1 (0.1%). The number of classic cesarean sections showed a definite decrease in the more recent period. In the period 1930-1934, it was performed on 78.2% of the patients and in 1950-1956, on 15.3%. The number of lower segment sections increased from 21.2% in 1930-1934 to 84% in 1950-1956. The low classic incision was still preferred for some patients, e. g., when dense adhesions with the urinary bladder were present as a result of a previous cesarean section or in some patients with transverse or oblique position of the fetus. The cesarean hysterectomies were all performed for uncontrollable hemorrhage after extraction of the baby, except in one patient who had a carcinoma of the cervix.

The average maternal death rate was 3.9%. Although the maternal death rate has fallen in recent years as a result of the use of antibiotics and blood transfusion, there was not a single death after cesarean section in the earlier period. The cause of death was puerperal infection in 16 patients, and most of these were treated in the period 1930-1934. Shock (operative or due to hemorrhage) accounted for 16 other deaths, and in one patient on whom extraperitoneal cesarean section was attempted spinal shock developed soon after commencement of the operation and the patient died. In two cases death was attributed to the general anesthesia and in three to pulmonary embolism. One patient died of paralytic ileus, and in 13 others the cause of death was a complication of pregnancy. There were 165 fetal deaths in this period, an incidence of 12.3%, and in the period 1952-1956 it was 17.6%. This high fetal death rate was associated with antepartum hemorrhage. Of the 12 stillbirths in this period, 3 were associated with abruptio placenta and 6 with placenta previa. There were 43 neonatal deaths, of which placenta previa associated with pre-maturity accounted for 10. From 1952 to 1956, of a total of 55 deaths, asphyxia was the cause of 21, and 11 of these showed evidence of fetal distress before the section was performed. All of these mothers had had a trial labor. All the babies were asphyxiated at birth and died within the first 48 hours. Eight mothers did not have a trial labor. Their babies were asphyxiated at birth and died within 48 hours, except one who died of bronchopneumonia on the fifth day. In these cases, probably the general anesthesia was responsible for the asphyxia.

JAPAN

Tuberculosis.—Because tuberculosis affects so many young persons, it is one of the nation's most pressing health problems. A government report places the number of cases of active tuberculosis at 3,400,000 and of arrested disease needing close observation at 1,470,000. Patients who know they have the disease but refuse to be treated constitute a dangerous source of infection. Among those with active tuberculosis about 410,000 have open cavities and about 860,000 require sanatorium treatment. Some improvement in the situation in general has occurred in the past five years.

Use of Hospital Beds.—Dr. Hideguki Iwasaki reported that, although the general hospitals and especially the psychiatric hospitals are overcrowded, there is a growing surplus of beds in the tuberculosis sanatoriums. This is partly because with modern improvements in the treatment of tuberculosis the patients can be discharged much sooner than was formerly the case and partly because many patients with tuberculosis cannot afford sanatorium care. At present no provision is made to assist such patients with public funds. Since the general hospitals are best adapted to care for patients with acute diseases and ill adapted for the care of those with chronic illnesses, unoccupied beds in tuberculosis sanatoriums are being used for such patients.

PORTUGAL

Hormonotherapy for Tuberculosis.—Cordeiro Ferreira and co-workers (*Rev. portug. ped.* **21**:281-290, 1958) treated a large series of tuberculous patients with prednisone, in a daily dosage of 1 mg. per kilogram of body weight. All patients always received isoniazid and streptomycin as well. Definite improvement was obtained with steroid therapy in patients with tuberculous meningitis, miliary tuberculosis, and pleurisy. Local application of steroids in patients with tuberculous adenitis of the cervical lymph nodes also produced greater improvement than treatment without steroids.

Adrenals and Mammary Cancer.—Frazão and Botelho (*Rev. iber. endocrinol.* **28**:433-441, 1958) studied the changes in the adrenals removed from patients with advanced and generalized mammary cancer. The changes in the adrenal cortex and medulla were identical with those seen in the adrenals of animals subjected to stress. In the cortex, the zonal disorganization, spongy appearance, folicular formations, and increase in lipoid and cholesterol content were similar to those associated with hypertensive disease and other conditions of stress. Vacuolar degeneration of the medulla also corresponded to findings seen in animals subjected to stress.

UNITED KINGDOM

Influenza Vaccine.—British experts have produced a live virus vaccine against influenza, which is being tested on volunteers. If it proves effective and safe, it will provide a new protection for the population at large. An attenuated live virus has the advantages over a killed virus that it can be produced much more quickly and is easier to give. A smaller dose suffices. The killed vaccine is injected. The live vaccine can be sprayed into the nose and throat. Because it is more virulent, it should not be given to young children. Work on the new vaccine is proceeding at the National Institute for Medical Research. Promising results with a live virus were achieved by the Russians. The cost of protection is likely to be less than with the vaccines used hitherto, and it offers the least discomfort. Ample supplies of killed virus vaccine, which has been proved to give 60 to 70% protection, are available. Vaccination is especially important for expectant mothers and people suffering from cardiovascular, pulmonary, or metabolic diseases. All such people can be vaccinated under the National Health Service.

Colored Immigrants.—According to an annotation in the *British Medical Journal* of Oct. 4, about 190,000 colored people live in Great Britain. This is about one colored to 250 white, though the distribution of the colored people is notably uneven owing to the greater prospects of employment in the industrial cities. Of these 190,000, about 100,000 came from the West Indies (chiefly Jamaica) and 50,000 from India and Pakistan. Because members of the British Commonwealth are free to come here, no administrative machinery exists to keep a count of their exact numbers. There is no doubt that the current high estimate is a phenomenon of the last decade. Unrestricted immigration from any country, whatever the color of its inhabitants' skins, is likely to cause difficulties when the country they enter is already densely populated. The social evils of slum life are apt to spread and defy attempts at their eradication. Fraud and frustration appear, and the immigrants, uprooted from gay and friendly company, seek ephemeral friendship and sexual solace where they can find it. An additional problem, apparently specific to the migrants from Jamaica, is that in the West Indies marriage has largely given way, through a transitional stage of "faithful concubinage," to outright promiscuity. It is thus not surprising that many half-caste children and some full West Indian babies are found in our orphan-

ages. Indeed a quota of 4 colored children in 10 has already been filled in these orphanages in some parts of the country.

While the social prospects of these population movements are not notably favorable, the strictly biological prospects are obscure. There is a lack of precise knowledge about the long-term implications of the human genetic mixtures taking place in our times, partly because of the relatively slow rate of breeding in the human race and partly because experimental breeding is out of the question. Moreover, it is debatable what, if any, inferences about miscegenation in human populations can be drawn from animal experiments, and in particular whether heterosis, or hybrid vigor, can be detected. All would agree with the society's advocacy of more research into the results of race-mixing, for ease of travel is likely to increase rather than impede it. Nor can anyone doubt the need for more education of people in an appreciation of the qualities distinctive of unlike or alien nations. While the question of whether immigration to Great Britain from Commonwealth countries should be restricted has many features outside the immediate professional interests of physicians, it is one on which they are well equipped to provide evidence, and to judge dispassionately.

Health Insurance.—The Fellowship for Freedom in Medicine has persuaded the British United Provident Association (B. U. P. A.) to launch an insurance scheme to help cover the cost of private treatment by general practitioners. The scheme will become effective in January. While there are already several excellent schemes insuring against the costs of treatment in a hospital as a private patient, private clinic, or nursing home, and of specialist advice or investigation, this is the first insurance scheme to cover the cost of private treatment by a general practitioner. It will be restricted to those already insured under B. U. P. A.'s standard scheme (for such items as private beds and specialist fees) whereby for an additional rate a subscriber may obtain insurance for himself and his dependents for attendance by a private general practitioner and for minor operations. The cost of drugs is not included.

Healing by Clergymen.—The report of the Archbishop's Commission on the Church's Ministry of Healing stated that all healing was divine healing and that healing concerned the whole person as an interrelated amalgam of spirit, mind, and body. One does not treat sickness, one treats a sick person. Many diseases are spiritual in origin and according to the report at least 33% of the patients in hospitals need the ministry of a priest rather than a physician. The Bishop of Coventry, however, stated that healing did not always follow faith, nor was suffering always contrary to God's will. Many public healing services have fostered a false impression that God must heal. It is wrong to assume that death is necessarily a disaster. There is a danger in calling this ministry "faith healing" or even "divine healing." Physicians are just as much the ambassadors of God in His ministry of healing as are pastors and praying laymen. It is right to remind the clergy that they have a ministry of healing, but there is a danger that people may become preoccupied with what they call the ministry of healing to the total exclusion of every other kind of ministry. They must see it in its proper perspective in relation to the total aspect of their ministry.

The Bishop of Lichfield said that the medical profession was ready and anxious to receive a lead from the Church. Later a succession of speakers affirmed their belief in demons. Canon E. G. Burrough of Oxford University said that he was a profound believer in angels, and also in demons. He believed that many of the people who spent their lives in lunatic asylums were possessed with evil spirits rather than suffering from diseases of the brain. The Dean of Windsor said there was nothing in the creeds about belief in angels or demons. He pled for "a reverent agnosticism" on the subject.

Oral Penicillin.—In the *British Medical Journal* of Oct. 11, David Wheatley sent a questionnaire to 180 members of the Northern Home Counties Faculty of the College of General Practitioners regarding penicillin for oral use. Although such preparations have been in use for nine years, the value of this method of administration is still subject to controversy. Wheatley received replies from 85 members. Of these 78 gave penicillin by mouth, 70 used it for both children and adults, and the rest for children alone. The ratio of patients treated orally to those treated by injection over a 20-day period in May was 5:2. These results, coming from varied practices, were probably representative of national custom. This being so, more penicillin may now be given by mouth than by injection. Of the infections commonly treated orally with penicillin, tonsillitis and acute otitis media ranked high followed by acute bronchitis, pneumonia, and boils. These results reflected the common penicillin-sensitive infections met with in general practice, with the exception of severe deep-seated infections, such as carbuncles, which are probably best treated with injections of penicillin.

With regard to the preparations used, penicillin V appeared to be sweeping the field although benzathine penicillin in its liquid form still retained a place in the treatment of children. Combined penicillin and sulfonamide therapy was not particularly popular, only 18 of the 85 using it. Its indications were for such infections as pneumonia or others that failed to respond to penicillin alone. The dosage schedules used showed wide variations; 56 of the doctors gave 60 mg. of penicillin V every three to six hours for children up to 5 years of age and

52 gave double this dose to adults. The dose used for other preparations was two or three times the above for adults. This would seem to reflect fairly accurately the difference between the amount of penicillin V absorbed from the gastrointestinal tract and that of other penicillin salts. A four to five days' treatment for the infections listed was recommended by 66. One physician thought that oral administration was better than injection; 64 found the two forms comparable. Of those who thought oral administration not as good as injection, 2 probably used inadequate doses. More continued to give the drug by mouth rather than by injection despite their impressions of the relative efficiency of the two methods, probably because they found the oral preparation effective enough to allow its advantages to overcome any slightly diminished therapeutic effect. Most general practitioners appeared to be satisfied with the effectiveness of oral penicillin therapy.

Doctors' Plea Fails.—Mr. Maclay, secretary for Scotland, told the British Medical Association (B. M. A.) that he cannot join with them in presenting a special case to the Court of Session on the general practitioners' pay dispute. He had been asked to agree to the presentation of a case to test the validity of the Spens Report and the Danckwerts adjudication on doctors' remuneration. The B. M. A. had taken counsel's opinion and was advised that in Scotland there existed a "special case" procedure for which the consent of Mr. Maclay was necessary. In a letter to the Association Mr. Maclay stated that he made his decision because he believed with the Minister of Health that no contractual obligation existed between the government and the medical profession on remuneration, and because a Royal commission was considering the matter. A spokesman of the B. M. A. said that the rejection of the Association's offer had been made without Mr. Maclay asking to see the Association's draft of the stated case. Mr. Maclay had been less than candid in his reference to the letter of rejection of November, 1956. The letter said that if the B. M. A. was not prepared to accept the Minister's rejection, the matter could be brought before the courts for adjudication. The spokesman added that despite the fact that the suggestion of obtaining a legal decision on the disputed question came originally from the government, the Secretary of State had rejected this approach. It may be that the government is less confident about the probable result of the suggested legal proceedings.

Medical Maneuvers.—Striking advances in the technique of rescuing and treating men wounded in action have been demonstrated by the Royal Army Medical Corps. After a mock nuclear explosion, "seriously wounded" infantrymen were evacuated from the front line by relays of helicopters. Spectators watched the progress of an infantry battalion advancing to forward positions. While still short of their objective the nuclear missile burst on their flank less than a mile away. A smoke mushroom streaked with orange rose 300 ft. over the Surrey pine woods. When it dispersed the battlefield was strewn with "casualties." Survivors among the five highly qualified medical soldiers, who now form part of every infantry battalion, sprang quickly into action giving prompt medical treatment to the wounded. Within ten minutes two of the most severely wounded were being evacuated in a new midget helicopter. Soon larger Whirlwinds from the joint experimental helicopter unit at Middle Wallop brought doctors, medical equipment, and supplies, and evacuated the wounded at the rate of one every three minutes. As a finale the helicopters landed a field surgical team.

Helicopters are still inadequate for large-scale operations of this nature, but a type which Army Medical Services officers said they would like to use for casualty evacuation, the new 48-seat Fairey Rotodyne, made a demonstration run after the exercise. An unusual feature of the exercise was the appearance of 48 women, who made up the first and only field medical company staffed entirely by women. The unit was formed to prove that even if all male physicians and orderlies from a casualty clearing station had to go forward in an emergency, women could carry on.

Blood Groups in Cyprus.—While establishing a blood bank in Cyprus, Clearkin made blood tests on 10,000 of the population of the island (*Brit. M. J.* 2:939, 1958). He examined the distribution of ABO and Rh (D) blood groups among both the Greek-speaking and Turkish-speaking inhabitants of the island. Basing his conclusions on fully adequate population samples, he found little difference between the ABO and Rh (D) blood group distributions in the two groups, but in their ABO frequencies both groups differed from the Greeks on the European mainland, and resembled more closely the Turks and inhabitants of the Levant. Populations which within the last few thousand years have shared a common ancestry have similar blood group frequencies. Hence a difference in blood group frequencies is evidence that ancestries differ. It is thus surprising to learn that the Greek-speaking Cypriots do not appear to have Greek ancestry at all, and are in fact genetically more closely related to the Turkish Cypriots than to the Greeks. Whether these observations on blood groups will help solve the racial problem in Cyprus is another matter.

Work Study in Hospitals.—Work study and scientific methods of working are to be tried in the physiotherapy departments of 3,000 hospitals in the

National Health Service. Because these are among the busiest departments in most hospitals, and are so short staffed, it is hoped that work studies may increase efficiency. More than 100 heads of physiotherapy departments have just attended a conference at Westminster Hospital, London, to deal with the problem. Work study methods are already in use in many departments at this hospital.

Addiction to Freely Obtainable Drugs.—All drugs which it is thought can cause, or are likely to cause, addiction are obtainable only on a doctor's prescription. According to the World Health Organization committee on drug addiction, such addiction is a state of periodic or chronic intoxication, detrimental to the individual and to society, produced by the repeated use of a drug. The characteristics of addiction are an overpowering desire to take the drug and eagerness to obtain it by any means, a tendency to increase the dose, and a psychological and sometimes physical dependence on it. The sale of new drugs may escape being restricted, as they may be in use for some time before their addictive properties are discovered. Drugs that have either a euphoriant or sedative action are likely to cause addiction in predisposed persons. Three drugs obtainable in Britain without prescription have recently been reported to have addictive properties. They are carbromal, tincture of chloroform and morphine (Chlorodyne), and phenmetrazine. Carbromal, a mild hypnotic and sedative, is sold by pharmacists under a number of proprietary names or as a constituent of proprietary mixtures. Some patients who are advised to take one or two tablets containing carbromal daily eventually take 15 to 20. Addicts taking it may become stuporous and ataxic. Chlorodyne, which contains 1 mg. of morphine in a two-teaspoon dose, has long been used as a domestic remedy. Its use in Britain is unrestricted. A case has been reported in which the patient consumed 160 ml., or one-third of an ounce, of this tincture daily. This amount contains 16 mg. of morphine. Phenmetrazine is a weight-reducing drug that is being used by addicts in place of amphetamine, a restricted drug, although its euphoriant properties are not so great. It is suggested that all new drugs should be initially listed under the poisons rules until they are shown to be innocuous, at which time they may be released and obtained without prescription.

Anastomosis in the Coronary Circulation.—It is generally believed that in the coronary circulation anastomoses follow the occurrence of ischemic myocardial episodes, appearing where and when needed. This view is questioned by Laurie and Woods, who investigated the blood supply in both normal and diseased hearts of 150 Bantu patients (*Lancet* **2**:812, 1958). Working in a native reservation they were able to perform autopsies on 67% of the patients dying in hospital. Hearts were perfused after death with lead phosphate suspended in gelatin, and roentgenograms were taken of the coronary circulation. The coronary artery and its major vessels were examined microscopically. Of 200 such perfusions, only 150 were technically successful. Functionally significant anastomoses were found in 75% of normal hearts from patients over 4 years of age, but in only 23% of hearts from patients with chronic ischemic heart disease. Functionally significant anastomoses were found even in the hearts of some newborn infants with no cardiac disorder. One child 13 days of age had a complete anastomosis to the left circumflex artery and to the whole right side of the heart, shown by perfusion into the left descending coronary artery. The authors considered that if anastomoses form after an ischemic heart attack, as has been suggested, there would be insufficient time for these to develop, as the myocardium cannot survive more than 20 minutes if deprived of its blood supply. They believed that the most likely explanation is that most healthy persons have a functionally important coronary anastomotic blood supply at birth. This anastomosis probably protects some against ischemic heart disease and may modify this condition in others.

Reduction of Sputum Viscosity.—In chronic bronchitis the mucosa of the bronchial tree is abnormal and the mucus-secreting glands, which are overdeveloped, produce excessive amounts of an abnormally tenacious mucus. This is a good medium for bacterial growth and leads to superadded infection and purulent sputum. The viscosity of the sputum of the chronic bronchitic is proportional to its hydration and mucoprotein content. The latter consists largely of desoxyribonucleoprotein (DNP) fibers. Robinson and co-workers (*Brit. M. J.* **2**:119, 1958) showed that the viscosity of bronchitic sputum can be reduced, and the clinical condition of the patient improved, by the insufflation into the peribronchial tree of a dry powder containing desoxyribonuclease and chymotrypsin. The size of the particles is important because if they are too large they will not reach the peripheral bronchial tree and may be deposited in the pharynx and trachea. The ideal particle size is around 3μ. With use of fluorescent-labeled chymotrypsin it was shown by means of bronchoscopy that some of the particles reached the terminal bronchioles. Tests were made with the powder on 36 chronic bronchitics. The sputum was collected daily, measured, and examined for mucoprotein and DNP fibrils, color, consistency, and relative viscosity. In 86% of the patients the sputum showed decreased viscosity, and in 66% there was appreciable lysis of the DNP fibrils. In 67% there was subjective improvement,

which was pronounced in several. Sputum was expectorated more readily and physical signs, particularly dyspnea, improved in nearly 50%. The possibility of sensitization to the enzymes exists but appears to be remote.

Health Hazard from High-Power Radio Stations.—*The Times* reported that the operation of certain forward-scatter radio links to be set up in Britain under NATO arrangements may constitute a hazard to the health of the local community. Each of these high-power, two-way directional radio stations would have a sterilized zone in its beam extending a mile or so ahead of the station in the direction of the transmission. The public will not be allowed permanently in these zones, and any existing farms or homes in the immediate vicinity of the new radio stations would have to be evacuated. It is even suggested that "death rays" might be emitted in these new radio stations. The Ministry of Defense, on the other hand, minimized the danger and stated that there might be a slight radiation hazard from the introduction of new radio techniques and advised the fencing off of an area of about 40 yd. in depth in front of the transmitter cones. The matter is being taken up by the Medical Research Council, whose experts pointed out that the hazards are not as great as those of nuclear radiation. The energy emitted does not produce the same biological changes and as far as is known does not have any genetic effects on future generations. The Council stated that those who have been working with radar for nearly 20 years have not suffered from any ill-effects and that animal experiments show that this form of radiation must be of high potential to constitute a hazard to health.

Cytological Screening for Cancer of the Cervix.—A report from the Faculty of the College of General Practitioners of S. E. Scotland shows that the cytological detection of early cervical carcinoma can be readily undertaken in general practice, and that it is well worth while in view of the number of unsuspected cases of cancer brought to light. Twenty general practitioners took cervical smears from all women coming for postnatal examination, from postmenopausal women without a history of disease of the genital organs, and from as many women as possible in whom a complete medical examination was indicated. Cervical smears were taken from 1,000 women and the slides sent to Edinburgh University for pathological examination. There were 15 unsuspected positives; that is, those who had a healthy cervix on inspection and palpation, but whose cervical smear was either suspected of cancer or frankly malignant. Five atypical cases were also found. The average age of this group was 35½ years. These patients were immediately referred to a gynecologist for further treatment. Six underwent total hysterectomy, one was treated with radium, and the rest were still under observation, four of them having had the cervix amputated. This incidence of 1.5% unsuspected cases of cancer of the cervix detected in general practice was high. Figures from hospital surveys made in gynecologic departments were about half this. The general practitioners concerned were unanimous in their opinion of the value of the cervical smear as a routine screening test and considered that it should be part of every pelvic examination.

Cutting Health Service Costs.—Proposals for improving the National Health Service without increasing the cost were made in the first of a series of debates at the Local Government Conference in response to a paper by Sir Keith Joseph, M. P. Sir Keith referred to defects in the service and recommended that before going to the taxpayer for extra revenue, efforts be made to improve efficiency by modern management techniques. Specifying the drug bill in particular, he said that 10% of the total cost went for drugs and that a method should be found to make the public pay more of this cost. A false incentive was given by the relatively low charge of 14¢ for prescriptions when the prescribing cost alone was nearly 28¢. The charge must, however, be so arranged that it does not discourage recourse to the physician when necessary. The grievances of patients who wait hours at clinics to see a consultant for a few minutes were aired by Mr. P. Maybury, of Swansea, who said the consultants are not to blame as many are overworked. The system falls down for lack of coordination. Dr. Dulcie Staveley, herself a consultant who kept patients waiting, blamed the general public's lack of a sense of time, saying, "You can give them appointments and work out the average amount of time it takes to see them but you can't work out whether the average person will keep the appointment." Mr. W. Lindsay, vice-chairman of the East Sussex County Council, complained that benefits are given to people who do not need them. The patient should at least pay for his board and lodging in the hospital if he can afford to do so.

Mr. Walker-Smith, Minister of Health, described the service as generally efficient although methods of promoting efficiency are always being considered. When the Labor Government was in office not one hospital was in progress or planned. Today 10 are in progress and 11 planned; 31 major schemes of hospital extension and modernization are in progress, and 60 are planned. Regarding patients' waiting time the Minister said that a hospital could never be equated with a factory or the healing of the sick with the making of goods, but new techniques would be introduced where it was possible

without detriment to the care and treatment of the sick. Five times as much is spent on drugs to keep patients out of hospitals as on drugs in hospitals. This gives a double benefit. This does not mean that costs should not be curtailed as far as possible without detriment to the patient. The speed and stress of modern life has increased the ratio of mental to physical illness. More than 40% of the hospital beds are devoted to mental cases. This is a great problem and challenge. More of these patients should be treated in the community rather than the hospital. Old people must be helped not only to live longer but to remain fit and active. Greater emphasis must also be placed on the prevention of illness.

At a Conservative Party conference Mr. Thompson, Parliamentary Secretary, Ministry of Health, stated that the big economies people want in the Health Service can be made only by closing hospital beds, charging for doctors' visits, or scrapping important parts of the service. Those who urge a better service at lower cost should not ask for the impossible. He was replying to a motion which urged that, in view of the ever-increasing rise in Health Service cost, the efficiency of the service be investigated. Mrs. J. Adams said the greatest resentment was directed at the foreign nationals and others who do not need a passport to come here and reap the benefits of the service. She had found that nationals from 15 foreign countries had obtained help in one year. Mr. F. A. Tomlinson claimed that in the vacation months an ever-increasing number of so-called working men went sick and drew $28 from the National Health Service in addition to their regular pay. An ever-growing number also imposed on the service through bulk compensation for industrial injury.

Center for Spastics.—The only training center in the world set up especially to train spastics for work in industry was officially opened at Welwyn, Hertfordshire, about 18 months ago. Since its opening it has fitted 20 young men and women, at one stage thought to be untrainable, for industrial jobs. In the workshop carpentry, light engineering, printing, and other technical subjects are taught. The center has accommodations for 32 spastics between the ages of 16 and 25, and there is a long waiting list. When students arrive, many of them cannot read or write, and all have physical disabilities which make the simplest process a heavy task. As well as being taught the skills for "outside" jobs, they have to be taught how to live. Many have got into the habit of lying in bed for most of the day. Frequently there is nothing else for them to do, and they are in the way of other members of their families if they get up. The strict schedule of the center (set times for meals, work, and learning) gives them their first idea of normal working life. In many cases they are given their first hope of being able to take part in that life. Finding jobs for the trained students is the biggest problem and slows down the work of the center. Employers are sympathetic but wary and fellow workers are apprehensive at first. The man in the street is too often ignorant even of what spastic means. There have been a few total failures, but after 18 months this center has established itself as a realistic training ground doing a sound and valuable job.

Alcohol and Driving.—Drew and co-workers examined the effect of small doses of alcohol on driving skill (*Brit. M. J.* 2:993, 1958). The apparatus used was a "Miles motor driving trainer," in which the subject sits in a dummy car facing a translucent screen in a darkened room. Behind the screen is a perspex disk with a road scene painted on it and this is projected, very much magnified, on the screen by a lamp. As the driver operates the accelerator and steering wheel the car appears to progress along the road. The apparatus used gives the illusion of driving along a mile of road. The aspects of performance scored were accuray of tracking, speed of driving, and the control movements of steering wheel, accelerator, brake, clutch, and gear lever. Records were also made of the number of collisions with the side of the road that would be likely to happen under normal driving conditions. The subjects tested, 40 volunteers from the staff of the Road Research Laboratory ranging in age from 23 to 40 years, were given a 20% solution of alcohol flavored to disguise the alcohol content. The dose ranged from 0.2 to 0.65 Gm. of alcohol per kilogram of body weight. The alcohol level was determined in the blood, urine, and breath at intervals over a period of two and one-half hours. The peak blood alcohol concentrations from the doses given were about 20, 40, 60, and 80 mg. per 100 ml. and the ratio of urine alcohol to blood alcohol was 1.25 to 1. The best results with breath testing apparatus were obtained with one known as the "breathalyser," which gave values corresponding closely to the blood alcohol values. The other forms of apparatus either showed high constant errors or were difficult to use.

Performance began to deteriorate with blood alcohol concentrations of the order of 20 to 30 mg. of alcohol per 100 ml., corresponding to an intake of 0.2 to 0.3 Gm. per kilogram of body weight. The deterioration was progressive and linearly related to blood alcohol level. There was no evidence of a threshold effect. The impairment in performance was shown most clearly in the operation of the controls, particularly in the timing of steering wheel movements. Mean error showed an increase with an increase in blood alcohol, amounting to about 16% deterioration with a blood alcohol concentration of 80 mg. per 100 ml. Part of the increase in error was due to a significant tendency

for subjects to move toward the right of the road after taking alcohol. Mean speed showed no significant change after alcohol, although there were marked individual differences in speed. Age, sex, and previous driving experience and drinking habits showed no relation to individual differences in response to alcohol, but personality ratings, especially those relating to extroversion and introversion, were definitely associated with driving performance.

Extroverts did not change either speed or control movements much, though they were less consistent in control movements, but showed large increases in error. Introverts changed speed markedly, but it was not possible to differentiate between those who slowed down and those who speeded up. Control movements were also increased in introverts. Error increased in some and not in others, but the mean error score was significantly less than in the case of extroverts, who on the whole did not seem to be bothered by the extra stress imposed by alcohol. They drove at much the same speed as normally and made few additional corrective movements, but made much greater errors than introverts. They were less consistent in their behavior than the latter and deteriorated more rapidly. Introverts on the other hand appeared to strive to compensate for the effect of alcohol and to be anxious to demonstrate their efficiency. If anything they overreacted to the situation, made more corrective movements, and changed their speed markedly, some even slowing down in an attempt to achieve greater accuracy, although they did not necessarily do so.

BUSINESS PRACTICE

This is the tenth in a series of excerpts from the brochure on the Business Side of Medical Practice, prepared by the American Medical Association in cooperation with the Sears-Roebuck Foundation.

AS YOUR PRACTICE GROWS

As soon as it is financially possible, many physicians employ an office girl who can assume many of the routine duties of running the office, freeing the doctor to spend more time with his patients. She often serves as a combination office nurse, receptionist, secretary, and bookkeeper. She is particularly valuable in serving as the doctor's ambassador to his patients.

A few years ago an office aide was the exception rather than the rule—today four out of five practicing physicians employ at least one woman. This trend continues to increase as more doctors realize that managing a medical office means not handling all detail themselves but directing others to do much of it. Recent surveys point up the fact that physicians with office assistants can see more patients each day than doctors who go it alone.

As his practice grows, a physician may augment his office staff to include a registered nurse, in addition to a receptionist-secretary, a laboratory technician, or, perhaps, an x-ray technician.

Hiring an Aide

The first thing for a physician to consider when he reaches the point at which he is able to hire additional office help is "What duties do I want her to perform?" Depending on the kind of practice he has, some physicians may be primarily interested in a receptionist-secretary; others may prefer to employ a registered nurse who will spend a greater share of her time assisting with the medical side of the practice. Where a professional management consultant is available, it may be economical, in the long run, to seek such assistance in training office aides.

As a guide to physicians in hiring an assistant, Dr. Harold Mickelson, of Northeast Missouri State Teachers College, has worked up a list of more than 40 specific duties which an assistant might perform. His list is based on the results of a survey he conducted in cooperation with the American Medical Association to determine the ideal qualities, training, and skills of a medical secretary.

Here are just a few of the duties a girl often performs: (1) receives patients and office visitors; (2) answers the telephone; (3) makes appointments; (4) transcribes patients' medical records, histories, and similar data; (5) opens and sorts mail; (6) takes the doctor's letters; (7) prepares and mails financial statements to patients; (8) prepares insurance papers for doctor's signature; (9) pays office bills, makes bank deposits; (10) maintains daily and monthly financial records; (11) orders business and medical supplies; (12) handles office filing; and (13) operates equipment, such as mimeographs, in connection with the business side of the office.

On the medical side of the office she may (1) prepare patients for examinations; (2) weigh and measure patients; (3) take blood pressure, temperature, pulse rate; (4) assist the physician with minor medical procedures and surgery; (5) do routine laboratory tests and procedures; and (6) perform office "housekeeping duties," such as sterilizing instruments.

Depending on her particular type of medical training, she may operate such equipment as x-ray and electrocardiograph machines, give injections, or administer therapy of various types. However, the physician should always remember that he is responsible for the actions of any of his employees; all of her duties should be performed under his immediate supervision.

When the physician has prepared his own list of the duties he wishes his office aide to perform, his next step is to decide what kind of a woman he is seeking. He may want a young woman or he may prefer a more mature woman; he may have some personal preferences about educational background, special training, and personality qualities. The personality of the medical aide is of extreme importance. Because she is the doctor's key public relations person, she should be sincerely interested in people, friendly, and cheerful, as well as sympathetic and courteous. Her efficiency may be important, but it may be offset if she has the wrong kind of personality for the medical office.

How can a girl's personality qualities be determined? The doctor himself can rate her on appearance, voice, poise, intelligence, self-confidence, and similar personality qualities in his interviews with her. There are also interview guides and forms which a doctor can adapt to his own needs available from such companies as the Personnel Institute, 37 W. 47th St., New York, or the Psychological Corporation, 522 5th Ave., New York, if he wishes to use the job evaluation techniques of personnel experts.

There are many other qualities a doctor seeks in an ideal assistant. He looks for maturity, a quality not always determined merely by the age of the applicant. He searches for dependability, self-reliance, and composure, for he knows that there will be many times when he is out of the office and quick decisions about the way to handle a given situation must be made by the girl. She will need a sense of humor and patience to carry her through the difficult schedule of days, and she must be neat and accurate in all her duties. The ideal girl balances efficiency with personality.

Locating an Assistant.—When the doctor has carefully analyzed his own office needs, translated these into a detailed list of the duties he wishes an assistant to perform, and set down the personality qualities for which he is searching, he is ready to begin interviewing applicants. Where does he go to find job candidates who will qualify? Here are some suggestions: 1. Check with the local medical society and with colleagues who may know of girls seeking employment. 2. Check with local medical secretarial and medical assistant schools in the area. 3. Get the assistance of employment agencies. 4. Advertise in local newspapers or professional journals. 5. If there is a local medical assistants organization, contact its placement chairman. (A nationwide organization of doctors' aides, the American Association of Medical Assistants, now has state and local chapters in many states.)

In screening applicants, the physician should have each girl fill out a personal history form and should talk with her himself about her qualifications and the nature of the job. He will want to hold final interviews with the best applicants, and, when he narrows the selection down to one or two girls, he will wisely check with past employers for references.

Salaries.—Every young doctor is faced with deciding what to pay an aide. Few men establishing new practices are financially able to pay huge salaries. However, it is false economy to hire an unqualified girl merely because she will work for a small salary. Mistakes can be costly in a medical office and a poorly qualified office aide may even drive away patients.

The range of salaries for medical assistants varies around the country, just as do the range of physicians' incomes. A good general rule to follow is to pay on the same basis as a good secretary in business. Such information is easily obtainable from local employment agencies or from business friends who employ secretaries.

Though the doctor should have some salary schedule worked out before interviewing job applicants, he may find it necessary to alter it somewhat, depending on the experience, training, and personality of the girl he hires.

Some doctors prefer to employ a girl who has worked as a nurse in a local hospital or who has been employed by another doctor or just completed a training course in medical secretary–assistant work. Others prefer to take a young girl with relatively little training and teach her the job.

In addition to establishing equitable starting salaries, the doctor must also know when and how much to raise his employees' salaries from time to time in order to keep wages in line with those paid in the area and to provide continued job incentive. Too frequently raises are postponed until an assistant actually asks for a raise or becomes so dissatisfied she threatens to quit or actually does so. A raise in salary is an expression of appreciation for a job well done. With a comparatively small staff, some doctors find that individual salary raises from time to time are more effective than a blanket raise for all who work in the office. Some claim a raise is best given after an effective piece of work has been completed or just as the employee is leaving on her vacation. This garden-variety psychology is based on the premise that when an assistant leaves with an increased feeling of good will toward the office she will be anxious to return.

Other Job Incentives.—Most physicians offer sickness benefits, definite vacations, free medical care, and similar attractive benefits to their employees.

Some provide bonuses; others work out a percentage of collections arrangement for the girl who must follow up on collections, although this can lead to overaggressiveness on her part where patients are concerned. The physician is competing with industry and the business world for competent help, and consequently he, too, will find that fringe benefits are a real inducement in attracting well-qualified applicants.

Training an Aide

Too many doctors hire an office aide, then heave a great sigh of relief and say, "Now go to work." To do her job well she must be thoroughly trained in the specific office routine with her duties outlined clearly and specifically. A clear delineation of responsibilities must be made; this is especially important if a physician has more than one aide in the office.

Training an aide requires a liberal amount of understanding and patience. Some physicians even cut down on their case load to devote extra hours to the important training period, realizing that thoroughness at the beginning pays off later. The training period should emphasize showing, rather than merely telling the girl what to do. This entails explaining why certain things are done in the way they are done, rather than teaching by rote. A typed list of all her general duties and the schedule by which they are to be performed should also be provided the new girl.

Some doctors employ a girl for a trial period of a few weeks, so that both can see how the arrangement is working out. The moment a physician employs help, he becomes responsible for her social security deductions and payments, withholding tax deduction, workmen's compensation protection, and other insurances that may be required in his state. Information on these matters and the appropriate sources for the necessary forms is usually available from the county medical society.

If she handles patients' payments and bookkeeping duties, it is desirable to secure a bond for her, and it should be carefully explained that this is a protection for her as well as for the doctor.

During the training period, praise means a great deal to a girl who is trying to gain confidence on the job. She must be impressed with the importance of attention to detail and the absolute necessity for maintaining patients' office confidences. The doctor should correct her when she makes mistakes, but should not do so before patients. However, he should not expect her to learn everything the first day.

If the girl works out satisfactorily, she soon will become an important member of the office team and the doctor will wonder how he ever managed without his loyal, dependable office girl.

It is to his advantage to allow her occasionally to enroll in refresher courses sponsored by medical societies and medical assistants groups. He may even volunteer to pay her tuition for such postgraduate education, since in the long run it insures a better-run office and enhances the girl's pride in her work.

MEDICAL FILM REVIEWS

Life in a Cell: 16 mm., color, sound, showing time 13 minutes. Produced in 1956 by and procurable on purchase ($145) from World Wide Pictures, 4626 Van Nuys Blvd., Sherman Oaks, Calif.

The purpose of this film is to facilitate the teaching of the biological concepts of the basic life functions of a single-celled animal, the ameba. The film consists of a study, primarily by means of photomicrography, of a group of animals whose bodies are made up of just one cell, to learn how the basic life functions are performed in them. The biological concepts are considered in the form of questions: What does it mean to be alive? How can a single cell perform the basic life functions? How are the one-celled animals classified? Why are scientists interested in life in a single cell? Evidence is then presented that will direct the student toward scientific conclusions. This is an excellent film which would be very useful to create interest for discussion purposes. It is recommended for showing as a supplement to biology classes at the college and high school level. It could also be used at the junior high school level; however, for these classes considerable teacher supplement and vocabulary training would be required.

Cheiloplasty: Correction of Harelip: 16 mm., color, sound, showing time 24 minutes. Prepared by James W. Kelley, M.D., Tulsa. Produced in 1956 by Bud Woods Productions, Tulsa, for and procurable on loan from James W. Kelley, M.D., 204 Utica Square, Tulsa, Okla.

In this film, the method of operation for correction of harelip is demonstrated in detail and then the case of a 2-month-old child is presented. Each step of the procedure is shown, as well as the postoperative results. After this there is another demonstration of an operation done on an adult under local anesthesia. Here again, the steps of the procedure and the final results are shown. Included in the film are preoperative and postoperative photographs of several adults and children on whom cheiloplasty was performed. The techniques used are all acceptable and the photography is clear and allows the procedures to be seen easily. The sound and explanation are very good. The film can be recommended for general practitioners, pediatricians, and medical students.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Infarcts of the Pancreas. J. W. McKay, A. H. Baggenstoss and E. E. Wollaeger. Gastroenterology **35**:256-264 (Sept.) 1958 [Baltimore].

This report is concerned with pancreatic infarction in the absence of acute necrotizing pancreatitis. The cases comprising this study were found among the records of 21,481 consecutive autopsies performed by the section of pathological anatomy at the Mayo Clinic during the years from 1924 through 1955. A thorough study of the autopsy protocols, anatomic specimens, photographs, and histological sections was made in all cases of pancreatic infarcts. An infarct was defined as tissue which had become necrotic because of impairment of its blood supply. The necrosis usually was of the coagulation type surrounded by a "zone of reaction" consisting of hemorrhage, dilated capillaries, and leukocytic infiltration. All the infarcts included were the size of one lobule or larger. The term "focal parenchymal necrosis" was used to designate necrotic acini in clusters smaller than one lobule. The term "focal fibrosis" was used to describe localized, fairly well-delineated areas of fibrous tissue, as opposed to diffuse interlobular fibrosis. The term "massive infarct" was used to describe instances in which one-fourth or more of the pancreas was involved. The term "malignant hypertension" was applied to cases in which the patient, during life, had had severe sustained essential arterial hypertension associated with edema of the optic disks.

Since isolated regions of acute hemorrhagic necrotizing pancreatitis could be confused with infarction, all instances of fat necrosis in extrapancreatic tissue or excessive peripancreatic or intrapancreatic hemorrhage were eliminated. Any evidence of diffuse inflammation of the pancreas in regions not immediately adjacent to infarcts was considered to be evidence of pancreatitis, and such cases were not included. Microscopic areas of fat necrosis, however, either isolated or adjacent to infarcts, were not eliminated, since they likewise could be ischemic in nature. Forty-one cases were found that fulfilled the required criteria; this represented an incidence of 0.19%. It was found that infarcts of the pancreas are most commonly associated with diseases characterized by occlusive lesions of the arteries, such as periarteritis nodosa and malignant hypertension. The relationship between infarcts of the pancreas and acute necrotizing hemorrhagic pancreatitis is not entirely clear, but this study indicates that lesions of each type may exist independently of the others and can be distinguished by their gross and histological appearance. It seems probable that, in some instances, pancreatic infarcts may produce significant clinical symptoms.

Among the 41 cases of pancreatic infarction, occlusive lesions of the arteries were found in 30 with thrombi or lesions of the arterial wall or both and in 3 with emboli. In the 8 cases with no demonstrable arterial occlusion, there was terminally either shock or congestive heart failure or both, which may have contributed to the production of ischemic infarction of the pancreas. The finding of frequent association of pancreatic infarcts with malignant hypertension and the failure to find any instance of acute necrotizing pancreatitis in 100 patients with malignant hypertension, studied by Hranilovich and Baggenstoss, seem to indicate that acute necrotizing pancreatitis is rarely caused by pancreatic infarction.

Observations on Staphylococcus Albus Septicemia in Mice and Men. I. M. Smith, P. D. Beals, K. R. Kingsbury and H. F. Hasenclever. A. M. A. Arch. Int. Med. **102**:375-388 (Sept.) 1958 [Chicago].

Evidence obtained from cultures of blood of 9 patients affected with septicemia caused by Staphylococcus albus shows that this disease cannot always be dismissed as being due to contamination. A second culture should be taken, since overlooking a bacteremia due to this organism may have serious consequences for the patient. When the diagnosis of septicemia due to Staph. albus is made, it is necessary to determine the in vitro sensitivities of the isolated strain, as these sensitivities differ from strain to strain. The prognosis for the untreated patient is poor; therefore, prompt, carefully chosen, and prolonged antibiotic therapy is recommended. Death may occur late in the course of the disease, often unexpectedly, even though the blood stream has apparently been sterilized by treatment. Before the sensitivities are known, treat-

The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1949 to date only, and no photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

ment with novobiocin and chloramphenicol can be recommended, but it should not be started until in vitro sensitivity tests have been made to a wide range of antibiotics.

Predisposing factors were common in the patients with this disease, such as rheumatic fever, previous illnesses requiring operation, and other manifestations tending to impair the general condition. The sexes were affected in a ratio of 2 males to 1 female, which was similar to that for patients with septicemia caused by Staph. aureus. The symptomatology included dyspnea, cough, and sore throat. Some patients complained of a pleuritic type of pain; shoulder, knee, and ankle joints were most often painful; chills and rash were common. Involvement of the cardiovascular system was frequently found at autopsy. Experiments in mice with 3 strains of Staph. albus obtained from the blood of patients rarely led to the death of the animals and seldom produced obvious evidence of the disease. Further studies to solve the problem of this disease are recommended.

Haemorrhagic Capillary Disorder Associated with Antihaemophilic Globulin Deficiency. L. S. Valberg and G. M. Brown. Medicine **37**:181-196 (Sept.) 1958 [Baltimore].

An investigation was made on a large family group, many members of which suffered from one of the commoner inherited hemorrhagic disorders of capillaries. The great-great-grandfather of the family was an Italian fisherman who bore the name of Alfredo Purpura. He and all but one of his children migrated to America. In all, 278 members have been traced, and these comprise the entire family, save for possible descendants of the daughter who remained in Italy. Some of the 4th generation still bear the name Purpura, and some of these are affected by the disease. Laboratory investigation was carried out on 35 members of the family in 3 generations. Inquiry into a possible hemorrhagic disorder was made in 60 other cases. The information obtained on the others varied in completeness and accuracy. A history of abnormal bleeding was given by 15 persons, 5 males and 10 females. In one other case abnormalities were found in the laboratory which were similar to those found in the cases with a positive history of abnormal bleeding. The bleeding in affected members of the family was generally mild, though one 9-year-old boy died because of prolonged epistaxis. The most common cause of trouble was tooth extraction, and 12 of 16 persons had had significant bleeding after this type of trauma. Bleeding from minor cuts had been a problem in 7 persons and epistaxis in 5. Tonsillectomy had been accomplished without difficulty in 2 persons but had been followed by hemorrhage in 4. There were 4 cases of excessive bleeding after major surgery (discotomy, appendectomy and cholecystectomy, hysterectomy and appendectomy, and hysterectomy), but in 4 cases major surgery (thyroidectomy, renal lithotomy, exploration of elbow joint, and appendectomy) was carried out without reported complicating hemorrhage.

Summarizing the studies on this family and of a review of the literature, the authors say that the disease occurs in both sexes and is transmitted as a simple dominant independent of sex. For the most part the clinical features are mild. Typical findings include a variable prolongation of the bleeding time and a blood clotting abnormality characterized by variable clotting and prothrombin consumption times and a consistent abnormality in the thromboplastin generation test confined to the barium-sulfate-treated plasma. Evidence that the coagulation defect in this condition is antihemophilic globulin deficiency is supported by assay procedures for antihemophilic globulin and by evidence that antihemophilic globulin and the factor in normal plasma which corrects the defect in a patient's plasma behave similarly on storage, heating, freezing, cooling, ammonium sulfate saturation precipitation, dialyzation, barium sulfate or aluminum hydroxide adsorption, and Seitz filtration. The administration of fresh blood and prednisone in one patient improved the coagulation and vascular defects sufficiently to permit discotomy and spinal fusion.

Consideration of the patients studied and the report in the literature of cases of primary hemorrhagic disorder characterized by a normal platelet count and by a prolonged bleeding time or by abnormal capillary fragility (or sometimes by both) leads to the distinction of 3 major syndromes: (1) a pure capillary disorder; (2) a capillary defect associated with an abnormality in the humoral factors of the coagulation mechanism; and (3) conditions in which there is a capillary defect and an abnormality in platelet form and/or function.

A Study of Heart Disease in One Hundred Eight Hospitalized Patients Dying With Portal Cirrhosis. J. H. Lunseth, E. G. Olmstead and F. Abboud. A. M. A. Arch. Int. Med. **102**:405-413 (Sept.) 1958 [Chicago].

The incidence and type of heart disease were evaluated in 108 consecutive patients who had moderate to severe portal cirrhosis at the time of death. The ages of these patients ranged from 26 to 83 years, with a mean age of 57.4 years and a standard deviation of 13.7 years. Twenty-six were women, and 82 were men. The examination revealed that 52 patients (48%) presented portal cirrhosis associated with severe heart disease, which was arteriosclerotic in 26, hypertensive in 9, valvular in 5, and hypertrophic in 12. The latter 12 patients constituted a frequency of 32.4% of cardiac

hypertrophy among the 37 cirrhotics of this series who were found to have no clinical or pathological evidence of hypertension or valvular or arteriosclerotic heart disease. These patients presented a clinical picture of both heart and liver disease. Shortness of breath, edema of the legs, ascites, and chronic cough occurring in both conditions made the precise assignment of symptoms to either the heart or the liver difficult. Paroxysmal nocturnal dyspnea and orthopnea, more typical cardiac symptoms, called attention to the heart disease in 2 of these patients. The outstanding clinical characteristic of this type of heart disease appears to be the occurrence of cardiac enlargement in the presence of portal cirrhosis and in the absence of known causes for cardiac enlargement, such as hypertension, valvular heart disease, or arteriosclerosis. Seven of these patients had cardiac enlargement demonstrated either on physical examination or by chest roentgenogram. Tachycardia in the absence of fever or significant anemia should lead one to suspect cardiac involvement associated with portal cirrhosis. Apical systolic murmurs were heard in 5 of these patients without gross or microscopic evidence of valvular heart disease, and in at least 2 of these the murmurs were associated with significant anemia. Electrocardiograms gave evidence of premature auricular and ventricular contractions and intraventricular conduction defects of varying degree.

One of the most salient findings in this study was the fact that the idiopathic cardiac hypertrophy was significantly more frequent in patients with early and moderately advanced cirrhosis than in those with far-advanced cirrhosis. Cardiac hypertrophy in these patients was believed to be due to the increased cardiac output associated with peripheral vasodilation in the early stages of portal cirrhosis. These findings suggest that patients with portal cirrhosis not only have the common types of heart disease but also are apt to develop an idiopathic heart disease associated with portal cirrhosis itself.

Urinary Delta-Aminolevulic Acid and Porphobilinogen in Different Types of Porphyria. B. Haeger. Lancet 2:606-608 (Sept. 20) 1958 [London].

The author discusses whether the presence of some porphyrin precursor earlier than porphobilinogen in the urine might not be a more reliable criterion of the porphyria-carrier trait than the presence of porphobilinogen. Recently Mauzerall and Granick found that the precursor of porphobilinogen, delta-aminolevulic acid, was also present in large amounts in the urine of 2 patients with acute porphyria. They accordingly devised a method for quantitative determination of this substance. This method was used in making quantitative determinations of delta-aminolevulic acid and of porphobilinogen in urine from 50 healthy adults, from 50 healthy children (aged from 7 months to 14 years), from 34 patients with acute intermittent porphyria, and from 128 of their closest relatives, as well as from 12 patients with porphyria cutanea tarda.

All patients with latent or manifest acute intermittent porphyria showed a pathologically increased excretion of porphobilinogen in the urine. This, therefore, appears to be an obligatory diagnostic sign. In two-thirds of the patients the excretion of delta-aminolevulic acid was also increased. In all apparently healthy but genetically certain carriers of the disease, the urinary excretion of porphobilinogen, and usually of delta-aminolevulic acid as well, was increased. This suggests that the disease can be transmitted only by persons with latent or manifest porphyria. A third of the apparently healthy children (below 15 years of age) of patients with latent or manifest acute intermittent porphyria had biochemical disorders suggestive of porphyria. It is noteworthy that so many of these children had latent porphyria, since manifest porphyria is very rare in this age-group. In patients with porphyria cutanea tarda the urinary excretion of delta-aminolevulic acid and of porphobilinogen followed no regular pattern. Determination of the porphyrin content of the urine and feces thus appears more useful in the biochemical diagnosis of this type of porphyria.

Peripheral Vascular Complications in Diabetes Mellitus: A Survey of 3,600 Cases. D. W. Kramer and P. K. Perilstein. Diabetes 7:384-387 (Sept.-Oct.) 1958 [New York].

The authors studied the problem of the relationship of diabetes mellitus and the incidence of peripheral vascular complications in 3,600 patients with diabetes mellitus seen in private practice and in hospitals in Philadelphia between 1921 and 1956. The ages of the patients ranged from 10 to more than 80 years, and their cases varied from potential to severe type. A progressive rise in the incidence of peripheral vascular complications from 8.8% between 1921 and 1930 to 47.3% between 1952 and 1956 was observed. This finding prompted the authors' attempt to obtain more information about the factors involved in the relationship of diabetes to peripheral vascular disease by examining the cases of 1,600 patients, observed between 1942 and 1956, according to duration of the diabetes, severity of the disease, age, and sex. Results showed that duration of diabetes alone is not a significant factor. The highest incidence of complications of the peripheral arterial system was in patients with diabetes of 1 to 5 years' duration. The next highest occurred in patients with diabetes of 6 to 10 years' duration. Similarly, the severity of the diabetes is not a definite factor, because the vast majority of

complications have occurred in patients with milder forms of the disease. Age and sex do not offer any significant explanation for the rise of the incidence of vascular complications. The findings of the survey suggest that the basic cause for atherosclerosis might best be sought in other fields. Further investigations in the field of metabolic disorders, besides cholesterol and carbohydrates, may give added information.

Sarcoidosis of the Spinal Cord: Report of a Case with Remission Associated with Cortisone Therapy. A. Moldover. A. M. A. Arch. Int. Med. **102**:414-417 (Sept.) 1958 [Chicago].

While sarcoidosis is a relatively common disease, involvement of the spinal cord, which occurred in a 24-year-old man with sarcoidosis, is so rare that the case appears to be of interest. The patient noticed pain in his calves 5 months before he was first seen in consultation, followed by pain in his right hip and lower back. For the past two months he had had difficulty in walking a straight line; he could not stand on his toes, climb stairs, walk rapidly, or stand on one leg. One week previously impotency and difficulty in urination developed, and he consulted an urologist. The prostate was normal, but his urinary condition was diagnosed as a cord bladder. The patient complained of extreme general exhaustion and weakness.

Physical examination revealed a tall cachectic young man, walking with a shuffling gait, unable to lift his feet from the floor. A generalized lymphadenopathy, including cervical, axillary, and inguinal nodes, was found. There was no tenderness of the spinal column. Chest roentgenograms showed enlarged hilar lymph nodes and diffuse pinpoint opacities throughout both lung fields. The gastrointestinal series showed an enlarged spleen indenting the greater curvature of the stomach. Neurological examination revealed bilateral hyperalgesia, impaired sensitivity to pin prick and touch over the left saddle-seat area, normal abdominal but depressed cremasteric reflexes, and absent knee and ankle jerks. The Babinski response was normal. The protein content of the spinal fluid was 128 mg. per 100 cc., and the sugar content was 40 mg. per 100 cc. An inguinal lymph node was removed for biopsy, and histological examination was consistent with sarcoidosis. The patient was treated with corticotropin in daily intravenous injections of 25 mg. (1 mg.=1.14 U. S. P. units); the corticotropin was dissolved in 500 cc. of 5% dextrose in water and was given slowly during 8 hours for 8 consecutive days. A dramatic response was obtained on the third day of treatment when bladder function was restored to normal; the patient was able to walk normally, the exhaustion disappeared, and he was discharged from the hospital in a much improved condition. All the symptoms and signs returned 6 weeks later, though, and the patient was then given cortisone by the oral route: 300 mg. the 1st day, 200 mg. the next 2 days, and 150 mg. for the next 10 days. The daily dose of cortisone was then reduced to 100 mg. Two days later insomnia developed, and a dose of 75 mg. was given. Two grams of potassium chloride was also administered daily. As before, the reaction to steroid therapy was excellent and was manifested by marked increase in appetite after administration of the first dose of the drug.

The disease in this patient was characterized by the alternation of prompt remissions when steroid therapy was given and relapses whenever it was stopped; after 2½ years of treatment cortisone was withdrawn. One and a half years after termination of the therapy, the roentgenograms showed for the first time normalization of the lung, the neurological findings were negative, and the patient resumed normal sexual activity. The results obtained with steroid therapy in this patient with sarcoidosis indicate its value in this condition.

Familial Congenital Hyperplasia of the Adrenal Cortex. G. Birke, E. Diczfalusy, L.-O. Plantin and others. Acta endocrinol. **29**:55-69 (Sept.) 1958 (In English) [Copenhagen].

The authors report on a family consisting of the parents, aged 47 and 44 years, and of 6 children, 3 of whom, aged 15 years, 12 years, and 8 weeks, had congenital hyperplasia of the adrenal cortex manifested as female pseudohermaphroditism; the other 3 children, 2 girls, aged 13 and 10 years, and 1 boy, aged 8 years, were normal both in weight and height and concerning their sex organs. Analysis of the steroid secretion in the urine was done in all 8 members of this family. The father, mother, and 3 healthy children showed a normal excretion pattern of 17-ketosteroids, 17-hydroxycorticosteroids, androgens, and estrogens. The youngest of the 3 female pseudohermaphrodites died before any steroid analyses could be carried out. The other 2 children with adrenocortical hyperplasia showed a substantially increased excretion of both 17-ketosteroids and 17-hydroxycorticosteroids as well as pathological changes of their excretion patterns. Androsterone showed a greatly increased output, but etiocholanolone could not be identified with certainty. The increased excretions of 11-oxy-17-ketosteroids consisted mainly of those of 11-keto-etiocholanolone and 11 beta-hydroxyandrosterone which were isolated and identified by infrared spectroscopy; 11 beta-hydroxyetiocholanolone could not be detected. An indirect analysis of the 17-hydroxycorticosteroid pattern revealed the presence of large amounts of pregnanetriol. Measurable amounts of pregnan-3 alpha,17 alpha,21-triol-20-one

(tetrahydro-S) were also observed in the urine. In neither of these 2 children was the excretion of the latter accompanied by hypertension. Tetrahydrocortisone and 11-keto-pregnan-3,17,20-triol were also identified, but no 11 beta-hydroxylated corticosteroids could be detected. The estrogen pattern was characterized in both patients by the complete absence of estriol. The older patient, who grew up as a girl, showed pronounced masculinization at the age of 14 and underwent bilateral subtotal adrenalectomy; after this operation substantial amounts of estriol were detected in the urine.

The assays in these 2 patients with adrenocortical hyperplasia thus revealed a partially new steroid excretion pattern characterized by the presence of tetrahydro-S despite the absence of hypertension, a defect in the 11 beta-hydroxylating mechanism, a dichotomy between androsterone and etiocholanolone excretion, and a disturbed estrogen pattern. These findings and those reported by other workers suggest very strongly that in congenital adrenocortical hyperplasia a number of different defects may arise in the enzymatic systems of the adrenal glands, more or less marked in different cases. Although a defect in the formation of hydrocortisone from its precursors appears to be a common factor in most of the patients with adrenocortical hyperplasia, various additional enzymatic defects, giving rise to different types of steroid patterns, also appear to be present.

Marfan's Syndrome. F. Erichsen and P. Svane-Knudsen. Ugesk. laeger **120**:1121-1126 (Aug. 21) 1958 (In Danish) [Copenhagen].

Arachnodactyly or congenital mesodermal dystrophy (Marfan's syndrome) designates a constitutional anomaly of hereditary character. In patients without cardiovascular complications or grave kyphoscoliosis, the prognosis for life is considered good. Since there is ectopia lentis in 50 to 75% of the cases, the state of vision often becomes decisive for the prognosis as to ability to work. Report is given on 9 patients with Marfan's syndrome whose typical cases have not previously been described. These patients represented 3 families, and information was also available on 10 relatives with the anomaly. Of the 2 patients with kyphoscoliosis, one died 2 weeks after the examination, probably of cor pulmonale. No cardiovascular lesions were demonstrated in the 8 surviving patients. Marfan's syndrome should be borne in mind, especially in mass examinations of school children or in the practice. Children with the anomaly can be helped by regular consultations with orthopedist and ophthalmologist and by advice as to choice of career. Many persons with the disorder are fully able to work, even at physically demanding occupations.

SURGERY

Leiomyosarcoma of the Stomach. L. W. Mason and V. R. Jablokow. J. Internat. Coll. Surgeons **30**:285-293 (Sept.) 1958 [Chicago].

The incidence of leiomyosarcoma of the stomach is about the same in both sexes, and the age of onset is usually one decade earlier than that of carcinoma. The prognosis after surgical removal (leiomyosarcoma is not a radiosensitive tumor) is relatively good. In this discussion 3 patients are alive and well 4, 7, and 8 years, respectively, after operation. Early diagnosis is extremely important and can be made by gastrointestinal hemorrhage, epigastric distress resembling peptic ulcer, a palpable epigastric mass, roentgenologic evidence, gastroscopic examination, and laparotomy. Distress is usually relieved by taking food and frequently by taking alkali in spite of achlorhydria (present in about 25% of cases). These tumors may vary from 2.5 to 25 cm. in diameter, are lobulated or nodular and rubbery, and may be found anywhere in the stomach, although rarely in the pyloric and cardial areas. They are usually less fixed and less hard and nodular than carcinoma. Roentgenologic diagnosis can rarely be accurately accomplished. In these 3 cases it could only be stated that a filling defect was present. Hypochromic macrocytic anemia is usually present, often in direct proportion to the duration of the disease. Usually there is no relation to gastric acidity. Free hydrochloric acid is lacking in the patient with leiomyosarcoma of the stomach more frequently than in the normal person, but it is much less common than in patients with carcinoma. Appetite usually remains good, and loss of weight occurs late or not at all. Many patients appear to be in good physical condition even in the terminal stages. The leiomyosarcoma is a slow-growing tumor, prone to metastasize late, although it infiltrates locally. It is usually encapsulated and spreads by displacement rather than by invasion.

Venous Shunts in the Surgical Management of Bleeding Esophageal Varices. R. W. Youngblood. J. Tennessee M. A. **51**:357-364 (Sept.) 1958 [Nashville].

The author reports on 9 female and 15 male patients with portal hypertension associated with esophageal varices who underwent 25 venous shunting procedures (11 portacaval and 14 splenorenal shunts) at the Vanderbilt University Hospital in Nashville, Tenn., between May, 1951, and March, 1958. Twenty-one of the 24 patients had intrahepatic block, and only 3 had extrahepatic block. Of the 21 patients with intrahepatic block, 12 had Laennec's or alcoholic cirrhosis, 5 had posthepatic cirrhosis, 3 had biliary cirrhosis, and 1 had cirrhosis whose cause was unknown. Of the 3 patients with extrahepatic block, 2 were children with thrombosis

of the portal vein secondary to omphalitis, and 1 was an adult with cavernomatous transformation of the portal vein. Preoperatively all patients except one had an average of 2 attacks of major hemorrhage. The surgical procedure usually consisted of end-to-side anastomosis with continuous, nonabsorbable suture material.

There were 2 operative deaths; one patient died 8 days and the other 15 days after the operation, both in hepatic coma. Three other patients died, one 8 weeks after the operation and two 4 years after the operation. Autopsies were performed on 4 of the 5 patients, and the shunt was patent in each of them. None died of hemorrhage. Only 2 other patients had subsequent bleeding during follow-up periods ranging up to 7 years; in one of these, bleeding followed thrombosis of a splenorenal shunt, the only instance of thrombosis in the entire series. The relatively low mortality rate and the rarity of complications and recurrent bleeding or thrombosis of the shunt are impressive when contrasted with older series of patients under nonsurgical management, who had mortality rates varying from 50 to 80%. Emphasis should be placed on the fact that bleeding is the most frequent cause of death in patients with esophageal varices. Therefore, venous shunting should no longer be considered as a palliative procedure, since other complications of cirrhosis may now be largely controlled with modern medical management. Portal-systemic shunts are feasible, with a low mortality rate even in poor-risk patients with cirrhosis. Liver function and ascites are infrequently improved by a shunting procedure alone but may be improved by medical means.

Transection of the Hypophyseal Stalk in the Management of Metastatic Mammary Carcinoma. G. S. Dugger, J. Van Wyke and J. F. Newsome. Am. Surgeon **24**:603-608 (Sept.) 1958 [Baltimore].

Hypophysectomy has been known to be followed by improvement in 50% of patients with metastatic breast carcinoma; however, total hypophysectomy is difficult and is not always achieved. The authors review attempts to achieve functional hypophysectomy, and, on the basis of experimental evidence, the procedure they used to cause a functional hypophysectomy consisted of transection of the infundibular stem or hypophyseal stalk and the placement of a disk of impervious material across the sella turcica. Thus, the revascularization of the hypophysis by vessels from the hypothalamus, specifically the vessels of the hypophyseal portal system, became unlikely.

Beginning in July, 1955, this operation was performed on 15 patients with advanced metastatic carcinoma of the breast. Endocrine function was assayed preoperatively and in the patients who survived sufficiently long postoperatively. Studies were made of the uptake of radioiodine (I^{131}) and protein-bound iodine, of the excretion of gonadotropins, 17-ketosteroids, and 17-hydroxycorticosteroids, and of the response of plasma 17-hydroxycorticosteroids to the adrenocorticotropic hormone. Six of the 15 patients with metastatic mammary carcinoma showed a remission, 4 gained no benefit, 1 died as a result of the operation, and in 4 patients the operation was too recent to permit evaluation. Average duration of remission was 6.6 months. This was less than that reported for total hypophysectomy but will probably improve with better selection of cases. Whether the quality of the remission is the same as that after total hypophysectomy has not been determined.

The Surgical Treatment of Cushing's Syndrome. F. Glenn, R. C. Karl and M. Horwith. Ann. Surg. **148**:365-374 (Sept.) 1958 [Philadelphia].

Thirty-two patients with adrenal cortical hyperfunction (Cushing's syndrome) have been evaluated during the past 24 years at the New York Hospital–Cornell Medical Center. All but 2 were women. The peak age of incidence was in the 4th decade. The most common physical complaint with muscular weakness or fatigue, which in 3 patients resulted in extreme disability. A 52-year-old woman had such severe muscular weakness that neurologists had entertained such diagnoses as muscular dystrophy and peripheral neuritis. Amenorrhea or menstrual irregularities developed in 24 of 28 women who were experiencing normal menstrual periods prior to the onset of their symptoms. A moon facies was noted in 25 patients, while truncal obesity with supraclavicular and cervicodorsal fat pads and thin tapered extremities occurred in 19. Facial and body hirsutism was frequently seen. Scalp hair tended to pull out easily. Atrophic skin, facial plethora, acne, and increased bruisability were common, but purple striae occurred in only 9 instances. Psychiatric problems varied from increased irritability to severe depression. Since an adequate method of determining serum and urinary 17-hydroxycorticoid levels has become available, this has been the most useful laboratory examination in the diagnosis of Cushing's syndrome. The 17-hydroxycorticoid values were elevated in 19 of the 22 patients in whom the test was employed, and the urinary 17-ketosteroid levels were increased in 15 of 28 patients. Other frequently encountered laboratory findings were diabetic glucose tolerance responses, eosinopenia, leukocytosis, increased insulin resistance, lymphopenia, alkalosis, and polycythemia. There were 14 instances of osteoporosis.

No satisfactory medical therapy is available for Cushing's syndrome, but excision of the hyperfunctioning adrenal cortical tissue has frequently induced permanent remission. Thirty of the 32 patients were operated on, the authors favoring a

lateral incision with resection of the 12th rib. Transabdominal exposure of the adrenal glands is reserved for patients with severe osteoporosis who cannot be placed in the lateral position without risking a compression fracture of a vertebral body and damage to the spinal cord. One of the first patients had what appeared to be normal adrenals, and only biopsy specimens were taken. This was a 9-year-old boy who subsequently underwent a spontaneous remission. Twenty patients had a total adrenalectomy. Nine patients underwent unilateral adrenal resection for either adenoma or hyperplasia. There were no deaths among the patients treated surgically. The duration of cortisone therapy varied from 2 days to several weeks in patients in whom adenomas were resected.

Within weeks after adequate surgical therapy, there is a redistribution of body fat, so that a more normal appearance is soon evident. Muscular strength slowly improves, and normal menstrual periods return. Osteoporotic bones gradually recalcify. The blood pressure often returns to normal levels. Although facial hirsutism usually subsides completely, it persisted in some patients. A persistent low-grade fever, sometimes accompanied by mild diarrhea, was experienced by some of the totally adrenalectomized individuals. In 3 patients who had both adrenals excised, transitory hypercalcemia and hyperphosphatemia developed postoperatively and was accompanied by such symptoms as fever, anorexia, nausea, vomiting, muscular weakness, polydipsia, and polyuria. In one patient, in whom all but a small remnant of adrenal tissue was removed, there developed 3½ years later a complete ophthalmoplegia on the right and bitemporal hemianopsia. The spinal fluid was bloody, and skull x-rays revealed an enlarged sella turcica which had not been present previously. Diabetes insipidus then became evident. A craniotomy was performed, and the clinical impression of a hemorrhage into a basophilic adenoma was confirmed. When adequate medical facilities are available, totally adrenalectomized patients can be maintained safely.

Cortisone as Cover for Major Surgery in Advanced Pulmonary Tuberculosis. J. R. Edge. Lancet 2:604-605 (Sept. 20) 1958 [London].

The author reports on 17 patients (14 male and 3 female) with far-advanced pulmonary tuberculosis for whom major surgery was considered to offer the only real hope of permanently arresting the disease. Their ages ranged from 26 to 58 years. The operations carried out were pneumonectomy in 5 patients, lobectomy in 4, local excision of cavity in 1, and thoracoplasty in 7. The patients have been followed up for from 6 to 21 months after operation. When the resting 24-hour 17-ketosteroid excretion was found to be low, cortisone therapy by mouth was started 3 days before operation in a daily dose of 100 mg. (25 mg. every 6 hours); this dosage was continued for a week after operation and then reduced, in weekly steps of 25 mg., to 75, 50, and a final 25 mg. daily. The total duration of treatment was 4 weeks. There were 3 postoperative deaths from definitive complications unrelated to stress. The remaining 14 patients had no postoperative complications, apart from transient basal collapse in one instance. The postoperative course was remarkably free of incident; the patients remained free of fever, dyspnea, hypotension, and tachycardia and on the day after operation looked and felt none the worse for the operation. The pink color and lack of any suggestion of dehydration were particularly striking. Wound healing proceeded quite normally in all patients. It is suggested that the replacement of deficient endogenous adrenal secretion contributed substantially to the recovery of the patients.

Clinical Aspect and Therapy in Patients with Tuberculosis of the Cervical Lymph Nodes. E. Beck, H. Behrendt and J. Kastert. Tuberkulosearzt 12:573-580 (Sept.) 1958 (In German) [Stuttgart, Germany].

The authors report on the results of combined surgical and tuberculostatic treatment in 949 patients, ranging in age from 10 to 60 years, with tuberculosis of the lymph nodes who were admitted to the sanatorium "Sonnenwende" in Bad Dürkheim, Germany, between 1949 and 1957. Treatment consisted of skin incision in the direction of folds of the skin, removal of the surface abscesses of caseous necrosis, and wide dissection of all palpable and visible subjacent lymph nodes. Roentgenograms before or during the operation helped to locate the calcified lymphomas. Complete extirpation of all caseous lymph nodes is necessary in order to guarantee a complete cure. Preceding the closure of the wound, streptomycin (0.5-1.0 Gm.), isoniazid (0.25-0.5 Gm.), and penicillin (200,000-400,000 units) were applied to the wound. Tuberculostatic therapy with streptomycin and isoniazid was started 3 to 5 days before the operation and was continued for the whole period of hospitalization. After the operation amithiozone (Conteben) was substituted for streptomycin, but, if liver damage existed, aminosalicylic acid (PAS) was used; cycloserine was recently given a trial.

Of the 949 patients, 553 had received previous treatment, while 396 had had no treatment. In 50% of the pretreated patients no tuberculostatic therapy had been given, and in 70% tonsillectomy had been omitted. Two hundred forty-five patients had received irradiation treatment without any success, and in 97 fistulas had developed. In all patients who had received irradiation treatment, connective tissue changes occurred and rendered operation

more difficult. All the patients who had received previous irradiation still had palpable lymph nodes which made surgical treatment necessary. Of 450 patients with involvement of one group of lymph nodes, 447 obtained complete cure, and 3 had recurrences. Of 222 patients with unilateral generalized lymph node involvement, 165 obtained complete cure, and 10 had recurrences. Of 112 patients with bilateral generalized lymph node involvement, 80 obtained complete cure, and 7 had recurrences. Of 41 patients with involvement of several groups of lymph nodes in nonadjacent areas of the body, 37 improved, and 4 had recurrences. The incidence of recurrence depended more on the extent of the tuberculous process, i. e., the number of groups of lymph nodes involved, than on the more or less advanced stage of the lesions; the incidence of recurrence definitely depends on the possibility or impossibility of complete surgical removal.

Early surgical intervention is recommended, not only to prevent disfiguring scars but also to shorten the toxic contamination of the entire organism by the tubercle bacilli. Irradiation therapy has lost its value in an era in which operative removal of tuberculous foci has become possible with the aid of tuberculostatic agents.

Tumors of the Carotid Body (Chemodectomas). E. Lima Basto. Arq. pat. **30**:305-334 (July) 1958 (In Portuguese) [Palhava, Lisbon].

Tumors of the carotid body, so-called chemodectomas, are rare. As a rule, they appear in persons of either sex, between the ages of 20 and 50 years, are unilateral (on the left side of the neck), and are either unilobular or multilobular. Externally the tumor grows very slowly, but internally it causes massive involvement and compression of the carotid artery and its bifurcation, the nerves, regional lymph nodes, the muscles, larynx, and pharynx. These tumors are histologically benign, but they may become malignant and result in metastases. Radium and roentgen-ray treatments are ineffective. The best treatment is surgical.

Three men with tumor of the carotid body were observed at the Hospital of the Instituto Portugués de Oncologia, of Lisbon, during the period 1956-1957. They were between the ages of 19 and 35 years. One of the patients occasionally had convulsions on the left side of the face and in the left arm. The tumors had appeared 5 or 6 years before consultation. They were unilateral and about the size of an orange. The cervical and submandibular lymph nodes were enlarged in all cases. Biopsy of these nodes showed either chronic lymphadenitis or atypical forms of lymphogranuloma. There were no metastases in any of the patients.

Operation consisted of dissection of the tumor, with conservation of the carotid artery in one patient in whom it was found that the tumor was causing compression of the carotid artery without entering its wall. In the other 2 patients, the tumor had involved the carotid wall; the carotid artery was ligated and resected in order to make possible complete extirpation of the tumor. There were no postoperative deaths. After the operation 2 patients continued in good health. The patient who had occasional convulsions before the operation was hospitalized 6 weeks afterward with a syndrome of intracranial hypertension. A decompressive craniotomy failed. An autopsy showed multicentric diffuse gliomatosis. There were no cerebral metastases of the tumor of the carotid body. The author advises an early operation before the tumor involves the carotid.

Primary Chief-Cell Hyperplasia of the Parathyroid Glands: A new Entity in the Surgery of Hyperparathyroidism. O. Cope, W. M. Keynes, S. I. Roth and B. Castleman. Ann. Surg. **148**:375-388 (Sept.) 1958 [Philadelphia].

Originally hyperparathyroidism and an adenoma of a parathyroid were regarded as synonymous, since, until 1933 no other type of anatomic disorder of the parathyroid glands was reported in patients with hyperparathyroidism. Beginning in 1934 and subsequently, other lesions of the parathyroids have been recognized. Since 1952, 10 patients with primary hyperparathyroidism have been encountered with a type of parathyroid hyperplasia distinct from adenoma, carcinoma, and the water-clear cell hyperplasia. All the parathyroid glands are enlarged by the disease process, the cells are predominantly of the nonvacuolated chief-cell type, and the entity is being called "primary chief-cell hyperplasia." It is essential that the entity be recognized at operation if secondary operations are to be avoided. The enlargements are most readily confused with adenoma, especially if only one gland is exposed. Five per cent of the first 200 patients with primary hyperparathyroidism cared for at the Massachusetts General Hospital in Boston have turned out to have this condition.

Four of the 10 patients with primary chief-cell hyperplasia also had tumors of the pancreas and pituitary gland, and it is suspected that this condition, previously described as "adenomatous hyperplasia" and "multiple adenoma," will prove to be the common type of parathyroid disease in patients with multiple endocrine abnormalities. Grossly, the cut surfaces of the individual glands present an ill-defined nodularity, which is more evident microscopically. The gross and microscopic appearance of a single gland may be insufficient to distinguish chief-cell hyperplasia from adenoma, and examination of all 4 parathyroid glands may be necessary to establish a definite diagnosis. The surgical treatment consists of total resection of 3 glands and a subtotal resection of the 4th.

Prescalene-Lymph-Node Biopsy. J. T. Wilson, E. G. Laforet, and J. W. Strieder. New England J. Med. 259:615-618 (Sept. 25) 1958 [Boston].

Prescalene lymph node biopsy was performed in a series of 153 patients with intrathoracic disease at Boston City Hospital. There were 148 cases in which lymphoid tissue was identified. Of these, 29 (20%) yielded histological evidence of the underlying pulmonary disease. Prescalene node biopsy was successful in 18% of the cases in which all other diagnostic methods short of exploratory thoracotomy had been unavailing. It is believed that, in view of the minimal risk, good diagnostic yield, and important prognostic significance, prescalene lymph node biopsy continues to be justified in the presence of intrathoracic disease. On appropriate indication the biopsy may also constitute a useful diagnostic adjunct in the patient who is hospitalized for pulmonary tuberculosis. In the present series of 20 patients undergoing this procedure, positive diagnostic information was obtained in 7. The yield of significant histological data was highest when the underlying pulmonary disease was sarcoidosis and lowest when it was tuberculosis. Bronchogenic carcinoma occupied an intermediate position.

The major indications for prescalene lymph node biopsy in patients hospitalized for pulmonary tuberculosis are as follows: inability to obtain bacteriological confirmation of the diagnosis of pulmonary tuberculosis, thus indicating that search for nontuberculous disease be intensified; x-ray findings suggestive of bronchogenic carcinoma; delay in x-ray improvement despite adequate medical therapy; and unexpectedly good clinical condition in the presence of roentgenologically extensive pulmonary disease. Bacteriological study of the cut surface of the resected lymph nodes is occasionally of value and should be performed more frequently. Although not done in this series, mycologic study of the resected lymph nodes is also recommended when the diagnosis is obscure.

Syndrome of Left Ventricular–Right Atrial Shunt: Successful Surgical Repair of Defect in Five Cases, with Observation of Bradycardia on Closure. F. Gerbode, H. Hultgren, D. Melrose and J. Osborn. Ann. Surg. 148:433-446 (Sept.) 1958 [Philadelphia].

A membranous ventricular septal defect which has its major flow into the right atrium has been recognized for many years. Recent advances in intracardiac surgery have made it possible to close such defects. This paper describes the essential clinical features of 5 instances of left ventricular–right atrial shunt. All were successfully closed with the aid of extracorporeal circulation. The first patient was a boy, who was first seen at the age of 10 years for the evaluation of a heart murmur. At operation at the age of 15, a small septal defect was found penetrating the septal leaflet of the tricuspid valve near its margin of insertion. The heart was stopped and the defect repaired under direct vision. After closure of the atrial incision, ventricular fibrillation appeared, but this was effectively reversed by cardiac massage and electrical defibrillation. Four months after surgery, the boy was asymptomatic even during strenuous activity.

In the second patient, a girl, the mother had discovered a heart murmur when the child was 18 months old. Operation at the age of 10 years revealed a defect in the upper margin of the septal leaflet at the tricuspid valve. This defect could be closed easily with the index finger, eliminating the thrill, slowing the heart, and raising the systemic blood pressure. It was decided that this lesion could best be corrected with the use of extracorporeal circulation. The operation was, therefore terminated and the patient allowed to recover. At the second operation, 8 months later, with the aid of extracorporeal circulation, the opening between the left ventricle and the right atrium was closed with interrupted sutures. There was also a defect in the upper margin of the septal leaflet of the tricuspid valve directly overlying the opening. The atrium was repaired and the heart restarted in normal sinus rhythm. There has been a remarkable improvement in physical capacity.

The third patient, a 5-year-old boy, had severe symptoms due to plumonary congestion, and there was doubt whether or not he would survive. Postoperatively he has shown remarkable improvement. The fourth patient was a 42-year-old man. He had severe cardiac symptoms; the physical signs were a ventricular septal defect. Catheterization data suggested an atrial septal defect. Postoperative recovery was uneventful, and there was no residual murmur. The fifth patient, a 17-year-old Eskimo girl, had a left ventricular–right atrial shunt which on catheterization was interpreted to be a ventricular septal defect.

The high ventricular septal defect associated with a defect of the septal leaflet of the tricuspid valve allows left ventricular blood to enter the right atrium. Of unusual interest was the finding that on manual closure of the defect there was a bradycardia and rise in systemic blood pressure. This phenomenon, previously described by Nicoladoni and Branham on closure of a peripheral arteriovenous fistula, has been thought to be due to the elimination of the reduced peripheral resistance at the fistula, which allows the full output of the left ventricle to pass into the systemic circulation. This causes stimulation of the carotid sinus mechanism and the depressor nerves, which then reflexly, through the vagus, slows the heart. It is believed that the effect shown here is similar physiologically to that observed on closure of an arteriovenous fistula, for the left ventricular–right atrial shunt is essentially an internal fistula. This phenomenon was observed in all 5 patients operated on.

Surgical Considerations of Occlusive Disease of the Abdominal Aorta and Iliac and Femoral Arteries: Analysis of 803 Cases. M. E. De Bakey, E. S. Crawford, D. A. Cooley and G. C. Morris Jr. Ann. Surg. 148:306-324 (Sept.) 1958 [Philadelphia].

This report is concerned with observations derived from an analysis of surgical experience during the past 5 years with 803 cases of occlusive disease of the aorta and iliac and femoral arteries. The obstructing lesion in chronic arteriosclerotic occlusive disease of the lower extremities was usually well localized and segmental in nature. There were 2 major groups of lesions, namely, aortoiliac occlusion and femoral occlusion. In the former group of 448 cases, 44% were characterized by complete aortic occlusion and 56% by incomplete occlusion. Associated occlusive disease of the peripheral arterial bed was present in 18% of these cases and was more frequently encountered in patients with incomplete aortic occlusion. Arteriographic studies were important in providing precise knowledge concerning location and extent of occlusive process to permit effective therapy.

Treatment of aortoiliac occlusive disease was directed toward restoration of normal circulation. Three types of surgical procedure were employed, namely, thromboendarterectomy, excision with graft replacement, and bypass graft. It was found that the indications for each of these procedures were dependent on location, extent, and nature of the occlusive process as well as on certain systemic factors; lumbar sympathectomy was a desirable supplemental procedure when there was associated peripheral disease, with secondary narrowing or occlusion in the smaller distal part of the arterial bed. The results of surgical treatment in aortoiliac occlusive disease were excellent. Circulation through the major arterial channels was restored in about 95% of the patients. Associated cardiac and renal disease constituted the major cause of operative mortality in 2.7%. Cardiac disease, mostly in the form of coronary thrombosis, was also the primary cause of death among the 9 patients whose late deaths occurred from 1 to 30 months after discharge from the hospital. The long-term results in these cases of aortoiliac occlusion have been satisfactory, as evidenced by the fact that recurrent occlusion was encountered in only 8 patients after varying periods ranging from 3 to 27 months. In all but one of these patients, who refused operation, the circulation was restored by a second operative procedure consisting of a bypass graft.

The pathological features of femoropopliteal occlusive disease vary, but certain patterns may be recognized. They may be classified into 3 groups: (1) those in which the occlusive lesion is discrete and well localized with relatively normal arterial elements above and below the occlusion; (2) those in which the process involves a considerable portion, if not most, of the superficial femoral artery but with patency of the popliteal artery and the distal part of the arterial bed; and (3) those with still more extensive and diffuse obliterative disease extending well down into the smaller vessels of the calf. Arteriographic studies are essential in the recognition and in the surgical treatment. Patients in the first 2 groups are amenable to treatment directed toward restoration of normal circulation, whereas those in the third are not and may be best treated by lumbar sympathectomy. Thromboendarterectomy may be satisfactorily employed in those in the first group, but in the second the bypass graft is the procedure of choice.

Of the 353 patients with occlusive disease of the femoral artery, 90% were treated by means of the bypass graft. Excision and graft replacement, which was employed in 19 cases in the early period of this experience, has been virtually abandoned in favor of the bypass graft. Endarterectomy is still considered a desirable procedure, but conditions in which it is indicated are rarely observed. Despite the greater difficulties imposed by this form of occlusive disease as compared with the more proximal form, the results of treatment have been gratifying, with restoration of normal pulsatile circulation in 84% of the patients. Long-term results were also satisfactory, as evidenced by the fact that recurrent occlusion was observed in only 14% of the patients over a period of 3 weeks to 38 months after discharge from the hospital. A second operation was performed on 27 of the 41 patients with late failure, and restoration of circulation was achieved in 20 patients.

Primary Splenic Pancytopenia: Dramatic Effect of Splenectomy. J. Tapie, J. Monnier, J. Poulhes and others. Presse méd. 66:1389-1392 (Sept. 13) 1958 (In French) [Paris].

The beneficial effect that may be exerted by splenectomy in patients with primary splenic pancytopenia was strikingly illustrated in the case of a 16-year-old girl whose life was endangered by repeated hemorrhages. The combination in this patient of febrile anemia, moderate enlargement of the spleen, and a hemorrhagic syndrome suggested the diagnoses of cryptoleukosis, aplastic myelosis, and hemorrhagic aleukia (aplastic anemia). Blood studies showed impoverishment of the 3 blood elements, i. e., isochromic anemia (red blood cells, 1,840,000 per cubic millimeter), leukopenia, and neutropenia, and an absence of platelets. Cold autoantibodies were also demonstrated. The diagnosis of leukosis was eliminated by the myelographic picture, which was practically normal, revealing an abundance of myeloid cells that contrasted strangely with the peripheral pancytopenia. The discrepancy between the findings in the peripheral blood and the appearance of the bone marrow

suggested the existence of hypersplenism, and the reduction of formed elements in all 3 blood lines completed the picture of primary splenic pancytopenia, as described by Doan and Wright.

Repeated transfusions, associated with vitamin K, vitamin B_{12}, iron given intravenously, and hormone therapy, failed to produce any lasting improvement, and the patient's condition grew steadily worse until at last splenectomy seemed to be the only means by which her life could be saved. The red blood cell count at this time was 1,580,000 per cubic millimeter and the leukocyte count was 9,600 per cubic millimeter. Energetic measures were taken, with the help of the Blood Transfusion Center, to improve this picture and to prepare the patient for the strain of operation. Transfusions of concentrated plasma increased the number of red blood cells per cubic millimeter to 4,250,000 by the end of 10 days, although the leukocytes numbered only 2,800 and the platelet level fell to 0. The operation was performed 5 days later and was followed by immediate cessation of hemorrhage and a rapid increase in the levels of platelets and the red and white blood cells. The patient left the service in excellent condition about a month after the operation: her skin and mucosa were normal in color; her temperature was 37 C (98.6 F); and she had already started to gain weight. Follow-up 3 months and 8 months later showed that the cure was apparently permanent and that she had every indication of perfect health, both clinically and biologically, although a few autoantibodies had reappeared in the blood.

An anatomicopathological study of the excised spleen revealed only discrete nonspecific lesions of a congestive character, without hemosiderotic overloading or fibrosis. Findings such as these obtained in this case are rare; they bring up the problem of the complex physiopathological mechanism governing the interaction of the spleen and the bone marrow, concerning which much uncertainty still exists. The theoretical aspects of this problem, however, interesting as they are, are eclipsed in practical importance for the clinician by its therapeutic implications. Primary splenic pancytopenia is one of the best indications for splenectomy, and this procedure should be resorted to without hesitation, even in apparently hopeless cases, if hormone therapy has been tried and proved unsuccessful.

Value of Laparoscopy in Ascitic Syndromes Presenting Diagnostic Difficulties. M. Girard and M. Coulot. Semaine hôp. Paris 34:2109-2115 (Sept. 4-12) 1958 (In French) [Paris].

Laparoscopy can now be more widely used because of the modern technical advances which have made the present-day laparoscope a highly developed and only slightly traumatizing instrument. Most French publications describe its value as a diagnostic procedure in conditions affecting the liver and gallbladder, especially jaundice, but this report is concerned with its use in patients with ascitic syndromes. The optical system of the laparoscope, unlike that of the cystoscope, is not designed for looking through liquids, particularly not ascitic fluid, which is rarely clear and transparent. The first requirement, then, is to evacuate the fluid and to dry the peritoneal cavity as completely as possible. This may be difficult, and, if it cannot be accomplished, the projected examination of the abdominal organs may become impossible. The second step is the creation of a pneumoperitoneum through the trocar used in evacuating the ascites. Anesthesia is then induced, plane by plane, with particular attention to the deep peritoneal plane. The small incision needed for the introduction of the trocar and the laparoscope is made with a bistoury at a site determined by the clinical conditions. The transmuscular route is preferable, provided that the course of the epigastric artery is respected, to the median aponeurotic route, which favors the development of postoperative ascitic fistulas. The Fourès laparoscope (diameter, 0.5 cm.), used by the authors, requires only a slight aperture in the muscle, which can easily be closed after the examination with 1 or 2 clips. A drop of collodion over the puncture-insufflation opening completes the operation, which is entirely benign and can be repeated 2 or even 3 times in the same patient.

The diagnostic value of this procedure was amply demonstrated in 32 patients with ascites studied by the authors, who summarize its advantages as follows: 1. Laparoscopy has a threefold importance in the diagnosis of hepatic sclerosis. First, it may show that the sclerosis is due to some cause other than alcoholism, e. g., by revealing the characteristic appearance of the hemosiderotic liver or of the macronodular liver of postviral sclerosis, or, as in one of the authors' patients, the presence of constrictive perihepatitis. Second, the general view of the liver parenchyma obtained by laparoscopy usually provides a better indication of the prognosis than any other clinical or histological guide. Third, laparoscopy alone makes it possible to deny, confirm, or reveal the existence of associated lesions, especially cancer or tuberculosis. 2. Laparoscopy alone in patients with ascites of tumoral origin but no perceptible tumor makes it possible to identify the true cause of the clinical picture (visceral cancer with or without peritoneal extension, primary or especially secondary cancer of the liver, or genital tumors in women). 3. Laparoscopy, supplemented when necessary by biopsy, is invaluable in establishing a diagnosis of peritoneal tuberculosis, sometimes showing the point of origin to be in the adnexa and indicating the type of treatment needed, whether medical or surgical.

Kidney Transplantation Between Seven Pairs of Identical Twins. J. E. Murray, J. P. Merrill and J. H. Harrison. Ann. Surg. 148:343-359 (Sept.) 1958 [Philadelphia].

The total experience with kidney transplantation at the Peter Bent Brigham Hospital in Boston is reviewed. In 16 of the 23 operations the donors were unrelated, and in none of these the transplanted kidney survived permanently. Fifteen pairs of monozygotic twins were observed as potential candidates for renal transplantation, and 7 received transplants from their identical twins. Four of these patients had chronic glomerulonephritis, 1 had subacute glomerulonephritis, and 2 had chronic pyelonephritis secondary to calculus disease and megaloureters respectively. Eight patients did not receive transplants; 3 of these died prior to treatment and testing, 4 still responded to standard therapy, and 1 refused to be considered.

The histories of the 7 patients in whom transplantation was performed are presented. Indications for the transplantation are that the healthy potential donor must have evidence of normal renal function bilaterally, be free from infection, have a normal lower urinary tract, and have sufficient understanding of the significance of a unilateral nephrectomy. The recipient must be in a terminal state of irreversible uremia and have a normally functioning lower urinary tract. The operative technique consists of 2 simultaneous operations, the nephrectomy and the transplantation, being started in 2 adjacent operating rooms. The nephrectomy on a healthy donor requires careful dissection of the vasculature to obtain maximum length of the renal artery and vein. The transplantation is accomplished with the patient under continuous spinal anesthesia. The recipient site is prepared in the right lower quadrant retroperitoneally, exposing the iliac vessels from the bifurcation of the aorta to the inguinal ligament. All the terminal branches of the hypogastric artery are dissected, care being taken to preserve each branch for possible use if renal anomalies are encountered in the donor. The renal artery is anastomosed end-to-end to the hypogastric and the renal vein end-to-side to the external iliac vein. If 2 or 3 renal arteries are present, suitable branches of the hypogastric are selected. The ureter is passed through a muscular tunnel and sutured to the bladder mucosa. The time lapse from clamping of blood supply in the donor to its restoration in the recipient has been 55 to 75 minutes.

Six of the 7 patients obtained return of normal function clinically, chemically, and by x-ray. One of these patients died 4 months after transplantation when the transplanted kidney became involved with the original disease. One other, still living, had signs and symptoms suggestive of active disease in the transplant. Four others are living and well, the longest 3½ years after transplantation. One recipient successfully completed a normal pregnancy a year and a half after transplantation.

NEUROLOGY & PSYCHIATRY

Papillary Carcinoma of the Choroid Plexus. J. Ribe Portugal and E. Geiger. J. Brasil. neurol. 9:91-111 (Jan.-Dec.) 1957 (In Portuguese) [Rio de Janeiro].

Tumors of the choroid plexus are extremely rare in children. As a rule, they are malignant. The treatment consists of surgical removal of the tumor and of roentgenotherapy. The surgical prognosis is poor. Recurrences are frequent and occur shortly after the operation in a high percentage of cases. The authors report the case of a child, 6 years old, who was hospitalized at the Hospital of the Instituto de Neurologia of the University of Brazil with an illness of 2 months' duration. The patient complained of frontal headache and vomiting. On hospitalization he was semicomatous and showed clinical and roentgenologic signs of intracranial hypertension, cerebellar symptoms, and sporadic clonic movements of the hands. The ventriculograms showed a tumor deeply located in the region of the left lateral ventricle. At operation the tumor was found in this ventricle, infiltrating and perforating the cerebral cortex at its middle line and spreading over the lamina quadrigemina and the superior cerebellar peduncles. After the tumor had been completely removed, histological examination showed it to be a papillary carcinoma. The patient did well after the operation and was discharged in satisfactory condition 2 months afterward.

According to the literature on tumors of the choroid plexus in children, these tumors have been located in the lateral ventricles in 32 of the 42 cases reported. The left lateral ventricle was more frequently involved than the right. Of the 42 cases, the tumor was found at autopsy in 24; 8 patients died postoperatively, and 10 recovered from the operation. One of the patients who recovered was a 6-year-old child. He is well and without any signs of recurrence 4 years after the operation. This case from the literature is similar to the one reported by the authors.

The Diagnosis and Treatment of Non-Traumatic Cerebrovascular "Accidents": With Special Emphasis on Intracranial Hemorrhage and the "Common Stroke." M. Scott. Pennsylvania M. J. 61:1190-1197 (Sept.) 1958 [Harrisburg].

Cerebrovascular accidents are fourth among the causes of all deaths (170,000 cerebrovascular deaths in 1952), and many more persons are partially or totally disabled by such accidents. The author defines a stroke as a symptom-complex that is most frequently caused by cerebral hemorrhage, throm-

bosis, embolism, or a brain tumor. The treatment depends upon the differential diagnosis, which can be reached by the following studies: careful history; physical and neurological examination; examination of the eyegrounds and perimetric fields; examination of the spinal fluid for pressure, color of fluid, cell count, quantitative protein, and Wassermann reaction; x-rays of the skull for evidence of shift of the pineal gland; and finally, after careful deliberation, cerebral angiography to decide between intracranial hemorrhage, vascular occlusion, and a brain tumor. Many persons with strokes due to small cerebral hemorrhages or thrombosed vessels recover spontaneously. The intramuscular administration of papaverine hydrochloride in doses of 100 to 200 mg. 4 times a day or the inhalation of 5 or 10% carbon dioxide in 95 or 90% oxygen is preferred treatment for cerebrovascular occlusion or embolism. The use of anticoagulants for suspected thrombosis can cause harm if hemorrhage is confused with thrombosis. Bleeding must be ruled out by a careful history, absence of hemorrhage in the eyegrounds and spinal fluid, and normal position of the pineal gland. The same precautions apply to the use of anticoagulants in cerebral embolism, but here they seem indicated.

The value of stellate block is uncertain. It should be done within 12 hours after the stroke by one skilled in its use and should be repeated 3 or 4 times at 12-to-24-hour intervals. Patients with cerebral aneurysm causing intracranial hemorrhage can be helped sometimes by ligation of the common or internal carotid artery in the neck or intracranial clipping of the aneurysm. Occasionally, patients with massive hemorrhages of the brain can be helped by prompt surgery with evacuation of the clot. The treatment should include therapy of the paralyzed extremity, treatment of speech defects, and management of the individual as a whole for ambulation and livable life.

GYNECOLOGY & OBSTETRICS

Myocardial Failure in Toxemia of Pregnancy. P. N. Siliquini and G. Garbagni. Minerva ginec. **10**:531-535 (July 31) 1958 (In Italian) [Turin, Italy].

The correlation between electrocardiograms and tissue oxygen utilization tests was studied in 53 patients with toxemia of pregnancy during the last trimester of pregnancy. The concurrent symptoms of the toxemia of pregnancy were edema, albuminuria, and hypertension. The degree of severity of the disorder was rated on the basis of deficiency in tissue oxygen utilization. Toxemia of pregnancy was rated as mild if the values of the tissue oxygen utilization test varied between 20 and 16%. In this group there were 23 women with a systolic pressure of 160 to 195 mm. Hg and a diastolic pressure of 90 to 105 mm. Hg. Electrocardiographic patterns did not change significantly during this moderate phase, as compared with those recorded before and after the clinical manifestation of the disease. Only a slightly increased cardiac frequency and moderate signs of a greater load on the left ventricle were observed. Toxemia of pregnancy entered a more severe phase when the values of the tissue oxygen utilization test varied between 15 and 11%. This condition was found in 18 patients with a systolic pressure of 150 to over 200 mm. Hg and a diastolic pressure of 95 to 135 mm. Hg. Electrocardiographic patterns showed changes due to the state of pregnancy or to the arterial hypertension in 11 patients. Myocardial failure characterized by smoothing of the ST segment and flattening of the T wave in all leads was observed in the electrocardiograms of 7 patients.

Toxemia of pregnancy was rated as very severe if the values of the tissue oxygen utilization test varied between 10 and 8%. These values were found in 12 patients, in whom a high degree of edema, albuminuria, and hypertension was observed. The systolic pressure of these patients ranged from 175 to 230 mm. Hg, and the diastolic pressure from 105 to 145 mm. Hg. Ten patients had episodes of eclampsia. Electrocardiographic patterns revealed the presence of diffuse myocardial failure during the acute phase of the disorder in 8 patients; they showed normalcy when the symptoms of toxemia subsided. Decompensation of the left ventricle was established in 3 patients. Since there was no evidence of heart disease in their past history, the decompensation was interpreted to be a manifestation of myocardial failure in toxemia of pregnancy. The decreased tissue oxygen utilization seemed to have been the main pathogenic factor of myocardial failure in this series of patients.

Uterine Carcinoma of Gartner Duct Origin. J. J. Andujar and F. E. Council. Texas J. Med. **54**:658-662 (Sept.) 1958 [Austin].

The authors report on 2 women, aged 20 and 25 years, with carcinoma of the uterus originating from Gartner's duct remnants in the organ. Both patients had a persistent vaginal discharge, and both were sterile. A large biopsy specimen was obtained from the younger patient, and a diagnosis of granuloma of the histiocytic type was made. Although the complete lack of mucin and the large, foamy, pinkish cells with an occasional cart-wheel appearance should have given a clue as to the nature of the lesion, an effort was made to cauterize the lesion on the right lip of the uterine cervix, and the patient refused further treatment. She died 8 months after the biopsy was performed, and autopsy was refused. Hysterectomy was performed on the second patient. The surgical specimen showed that the tumor occupied most of the cervix and endocervix and that it seemed to merge with the contiguous musculature of the uterus. Microscopic

examination revealed large cells of a rather pinkish color, with round or polyhedral edges. The nuclei were pale and slightly vesicular. In occasional rare fields one could see a cart-wheel pattern. There was no mucin elaborated. No evidence of metastasis was observed 3 years after the surgical intervention.

Gartner's duct remnants in the uterus may give rise to neoplasms. There is a wide difference in the reported incidence of such remnants. Of 1,716 uteri removed by complete hysterectomy and examined by the authors in an attempt to determine the incidence of these remnants by step sectioning the cervix and its vaginal portion horizontally at intervals of a few millimeters, reasonably characteristic Gartner's duct remnants were found in only 36, an incidence of almost 2%. A deceptive microscopic pattern and a lack of awareness of carcinoma of the uterus originating from Gartner's duct remnants may lead to an erroneous diagnosis. The benign appearance of the carcinoma was belied by its fatal course in the first patient. It is possible that the second patient was cured as a result of early removal of the uterus with tubes and ovaries, but survival for 3 years does not warrant a cure. Most of the patients whose cases were collected from the literature later had metastases and died despite the innocent appearance of the histological pattern of the tumor. This type of carcinoma of the uterus deserves far more attention and consideration from clinicians and pathologists in order to classify and combat it effectively and accurately.

Endocrine Relationships between Chronic Cystic Mastitis and Cancer of the Breast. N. A. Womack. Am. Surgeon 24:618-629 (Sept.) 1958 [Baltimore].

This report is based on an extensive review of the literature and on observations made in the department of surgery, University of North Carolina School of Medicine, and the North Carolina Memorial Hospital at Chapel Hill. The hormones having the greatest effect on breast structure are the estrogens, progesterone, and the lactogenic principle from the hypophysis, prolactin. In the breast these hormones work both synergistically and antagonistically. The numerous breast lesions that have come to be referred to as chronic cystic mastitis all represent variants of a single group of histological changes, e. g., duct growth as evidenced by epithelial hyperplasia, duct branching and increase in diameter, acinar atrophy, and periductal edema and fibrosis. At times there may be secretion within the duct; at times there is also round-cell infiltration. The dominant lesion, however, remains within the duct. Thus, it can be seen that chronic cystic mastitis has little to do with inflammation and frequently is not related to cysts. The term "chronic cystic mastitis," however, has reached such a fixed state in medical nomenclature that the author does not attempt to change it. Chronic cystic mastitis develops when a factor of initial susceptibility is followed by a period of long and constant uninterrupted estrogenic action. Chronic cystic mastitis is a conditioned process when not associated with permanent epithelial change. It is thus reversible, and this reversion can be brought about by the withdrawal of estrogen or the administration of an estrogen antagonist. Progesterone in adequate dosage seems to be an effective antagonist.

At the author's clinic progesterone in oil was used in treating 15 patients with chronic cystic mastitis. Pure progesterone in oil was given intramuscularly in 50-mg. doses, beginning about 2 weeks after the start of the previous menstrual period and on alternate days until the next period began. The use of progesterone in oil, because it necessitated several injections each month and was expensive, was not satisfactory. Neither was long-acting testosterone which, while an effective antiestrogen, possessed undesirable side-effects. More recently at the author's hospital hydroxyprogesterone caproate (Delalutin) has been used. This progesterone ester is given as a single intramuscular injection of 250 mg. The results obtained with it in 41 patients are tabulated. After 3 or 4 successive monthly injections treatment is stopped, and the patient is examined at intervals of 3 months. If cysts recur, a new cycle of treatment is begun. All treatment can usually be stopped after the menopause. Most patients treated with either hydroxyprogesterone caproate or progesterone in oil responded favorably to 3 or less monthly injections, the premenstrual breast pain and the nipple discharge being relieved. These observations, along with the fact that the cysts did not refill under therapy, suggest an effect on duct secretion. It is also of interest that 17 of the 56 patients treated had had previous surgical excision of the cystic disease before beginning hormone therapy.

The promoting factor for chronic cystic mastitis, namely, estrogen, also promotes the progression of breast cancer. If the initiating factor for the latter happens also to be present in a patient with chronic cystic mastitis, progression into cancer may occur. Statistical evidence suggests that women with chronic cystic mastitis stand a greater chance to develop breast cancer than do women without it. When cancer of the breast occurs, the withdrawal of sources of endogenous estrogens or the administration of antagonists, such as androgens, will be effective only to the extent to which the cancer cells are reversible.

PEDIATRICS

Ulcer Disease in Children. C. C. Hatfield. Virginia M. Month. 85:561-564 (Oct.) 1958 [Richmond].

The author presents the histories of 2 girls, aged 9 and 13 years, and of 2 boys, aged 14 and 17 years, who had a variety of abdominal symptoms and in whom investigation revealed duodenal ulcer. The children were observed in the course of less than

13 months. The 9-year-old girl exhibited typical ulcer symptoms, and the author feels that had she been 20 instead of 9, a diagnosis would have been made at the first office visit. The 13-year-old girl offered a more difficult problem since her symptoms were vague; she resembled the adult patient, with mild epigastric distress and vomiting without definite physical findings. The 17-year-old boy had an almost classical picture except for absence of relief by food; his symptoms were all referable to his gastric retention. The 14-year-old boy had typical ulcer symptoms for 2 years, with retention being the outstanding cause of complaint.

Ulcer disease in children presumably runs the same course as in adults. There is pain, hypermotility, gastric retention, food relief, flatulence, nausea, and vomiting. In the children of this series fluoroscopic examination proved of greater value in identifying the site than did the conventional plates. The use of a spot-film device aids in capturing the involved area at critical moments. It is well to remember that ulcer disease may appear at any age. Symptoms and signs are the same in children as in adults. Response to treatment is excellent. If the physician is aware of the possibility of ulcer disease in children and keeps it in mind, he will be able to diagnose the condition in many of these patients earlier and rehabilitate them more quickly.

The Incidence of True, Chromatin-Positive Klinefelter's Syndrome and Its Relationship to Feeblemindedness. A Prader, J. Schneider, W. Züblin and others. Schweiz. med. Wchnschr. **88**:917-920 (Sept. 20) 1958 (In German) [Basel, Switzerland].

The authors determined the nuclear pattern of sex in 336 boys, between the ages of 7 and 15 years, with mild feeblemindedness who attended special classes of the city school in Zürich, Switzerland, and in 390 boys with a high degree of intelligence who attended various high schools in eastern and central Switzerland and served as controls. Of the 336 boys in whom the nuclear pattern was determined with the aid of buccal smears, 8 were found to be chromatin-positive, i. e., their nuclear pattern was of the female sex but they were phenotypic males. The nuclear pattern of the leukocytes was also female in these 8 boys. These findings were sufficient for the diagnosis of true Klinefelter's syndrome. There was no doubt as to the correctness of this diagnosis, since the 2 oldest of the 8 boys had already reached puberty and showed the classic triad of this syndrome, namely, small testes, gynecomastia, and increased excretion of gonadotropin in the urine. Not a single one of the 390 high-school boys with high intelligence was found to be chromatin-positive.

The incidence of true Klinefelter's syndrome was estimated by other workers to be 1 in 10,000. In contrast to this estimated incidence, the authors' findings suggest an incidence of 1 in 42 in males with mild mental deficiency and of at least 1 in 1,000 in the entire male population, i. e., an incidence 10 times higher than the estimated one. The authors' findings prove that the previously observed frequent occurrence of mild feeblemindedness in patients with true Klinefelter's syndrome is not an accidental one. It justifies the routine determination of the nuclear pattern of sex in all mentally deficient males. Due to the fact that 6 of the 8 boys had not yet reached puberty, it was possible to study for the first time the somatic, electroencephalographic, and psychopathological aspects of the true Klinefelter's syndrome in childhood. Similar to the observations made in adult patients with this syndrome, 2 types of body build were seen in the prepuberal patients, namely, the type with inconspicuous proportions of the body and that with definitely eumuchoid proportions. The psychopathological aspect of mild feeblemindedness, mental infantilism, and passive personality was quite similar to that observed, as a rule, in adult patients. A marked psychoendocrine syndrome which was reported frequently in adult patients was apparently absent in the prepuberal patients. Abnormal electroencephalographic recordings were obtained from 4 of the 6 prepuberal patients.

Influence of Adrenal Cortical Hormones on the Course of Miliary Tuberculosis. A. Nitschke. Deutsche med. Wchnschr. **83**:1593-1595 (Sept. 12) 1958 (In German) [Stuttgart, Germany].

Earlier observations had revealed that glucocorticoids, such as cortisone, exert a favorable influence on tuberculous meningitis in childhood in that the sugar and chloride contents of the cerebrospinal fluid, which otherwise are reduced for periods of many weeks and which under the influence of tuberculostatic drugs increase only gradually, are elevated to a normal range within a few days after cortisone is given as an adjuvant. The increase in the sugar content of the cerebrospinal fluid can serve as a guide not only for the size of the cortisone dosage but also for the period cortisone treatment has to be continued so that the normalized sugar level will not decrease again.

The author used cortisone or prednisone in treating 9 children with miliary tuberculosis, of whom 4 had miliary tuberculosis without meningitis. It was found that the drugs had to be given over long periods and in large amounts. Doses of 3 mg. of prednisone per kilogram of body weight per day caused regression of the miliary foci in the lungs within an average of 20 days after the onset of treatment, so that they were no longer visible on roentgenoscopy. At the same time, the general condition, the fever, and the sedimentation rate of the erythrocytes were favorably influenced. Comparable series of children treated earlier only with streptomycin and isoniazid showed a similar regression of lesions much later, generally after more than 3 months. In children in whom meningitis complicated the miliary tuberculosis, the menin-

gitis usually subsided simultaneously with the miliary lesions, as was indicated by the sugar and chloride values of the cerebrospinal fluid. In children with miliary nodules in the eyegrounds (retinal involvement), the signs of acute inflammation rapidly regressed, leaving minute scars. The acceleration of the healing processes was so striking that the use of corticosteroids as adjuvants is recommended, provided that proper precautions are taken.

Pulmonary Atelectasis in Bronchial Asthma in Children. J. Luhr. Nord. med. **60**:1198-1199 (Aug. 21) 1958 (In Norwegian) [Stockholm].

Pulmonary atelectasis refers to roentgenographically demonstrable collapse of larger or smaller parts of one or both lungs. It is a relatively frequent complication in bronchial asthma in children. Roentgenograms of the lungs of 217 children with bronchial asthma who were treated in the Children's Clinic of the Rikshospital in 1951-1956 showed atelectasis in 12 children, most of them under 10 years of age. It was localized in one lobe, usually the middle lobe of the right lung. Roentgenologic clarification occurred after from 12 to 77 days. Three patients had relapses which persisted for 6, 19, and 106 days respectively. True allergy was seen in 7 patients; bacterial allergy, in 5. Atelectasis may occur in symptom-free periods but occurs more often during asthma attacks. It is ascribed to occlusion of one or more bronchi because of abundant, thick, tenacious secretion, edema of the bronchial mucous membrane, and spasm of the bronchial musculature. The prognosis seems to be good. Bronchoscopy with aspiration of secretion, and possibly the administration of antibiotics to prevent a secondary infection, may be necessary if the atelectasis does not recede quickly.

THERAPEUTICS

A New Superior Oral Diuretic Drug, Chlorothiazide (Diuril): Clinical Evaluation. C. R. Herrmann, M. R. Hejtmancik, R. N. Graham and R. C. Marburger. Texas J. Med. **54**:639-644 (Sept.) 1958 [Austin].

Fifty hospitalized patients with congestive heart failure and other diseases involving edematous and hypertensive states were treated with chlorothiazide (Diuril), a sulfamyl benzothiazide compound. The patients were on a low-salt diet (100 mg. per day), and most of them received 45 mEq. of potassium per day. At first, 250 mg. of chlorothiazide was given orally 1, 2, 3, or 4 times a day, and then the dose was gradually doubled for a total of 1 to 2 Gm. per day. The average 24-hour dose in these 50 patients was 750 mg. because of the low dosage used at the beginning of the therapeutic trial. At present 1.5 to 2 Gm. per day is given, and no toxic reaction has occurred, except for a mild rash in 2 patients, diarrhea in 1 patient (which may have been incidental), and hypopotassemia in 2 patients.

Chlorothiazide given orally in doses of 1 to 2 Gm. daily practically always initiated a diuresis within 1 or 2 hours, to reach a maximum at 4 hours and to continue for another 12 to 24 hours. The average duration of therapy in this group of patients was 14½ days, with a maximum of 66 days and a minimum of 2 days. The urinary output before the institution of treatment with chlorothiazide averaged 1,120 cc. per day, as compared with an average output of 1,725 cc. per day after the administration of the drug. The loss of weight in these patients over the average 14½ days of treatment was 15½ lb. (7 kg.). The output of the urinary electrolytes was quadrupled freqently in the first few days of chlorothiazide therapy. It then was maintained at doubled values for 5 to 7 days and remained elevated as long as the urine flow was increased. The patients in congestive failure excreted on the average 28.75 Gm. of sodium, 35.03 Gm. of potassium, and 29.5 Gm. of chlorides for the diuretic period averaging 14 days. The potassium output was unduly high as a result of the routine loading of potassium chloride.

Chlorothiazide thus proved to be highly effective in the treatment of edema. It is ideal for long-term therapy in patients with congestive heart failure except for those on a low-sodium diet and for those with hypertension, nephrosis, and cirrhosis. It may produce low serum potassium levels, and it seems desirable to administer 4 Gm. of supplementary potassium chloride daily, especially if digitalization or steroid administration is carried out. Chlorothiazide is particularly effective in patients with hypertensive atheromatous coronary ischemic heart disease associated with edema, and the drug is superior to all other diuretics, including organic mercurial preparations given by the parenteral route. Chlorothiazide is the drug of choice in eclampsia and in edema of pregnancy. Chlorothiazide appears to be the safest, most effective, and most practical diuretic that has been added to the armamentarium since mercaptomerin (Thiomerin) was introduced.

Experiences with Chlotride, an Orally Administered Nonmercurial Diuretic Used for Treatment of Cardiac Edema. R. Richterich. Schweiz. med. Wchnschr. **88**:906-910 and 931-934 (Sept. 13 and 20) 1958 (In German) [Basel, Switzerland].

Chlotride is the Swiss trade name for chlorothiazide (Diuril). This new diuretic sulfonamide with mercurial-like action is administered orally and enhances particularly the sodium and chloride excretion without producing any change in the excretion of bicarbonate in the urine. Often a slight increase in the urinary excretion of potassium may be observed. Three women and 2 men, between

the ages of 54 and 81 years, with acute congestive heart failure and extensive edema, 2 of whom were resistant to mercurial diuretics and acetazolamide (Diamox), were given orally 1 Gm. of chlorothiazide per day. Good diuretic results were obtained in all the patients. Undesirable side-effects were observed in only one patient who vomited once on several days; this patient also had a mild degree of hypochloremic alkalosis and showed signs of overdosage of digitalis (bigeminy) which disappeared spontaneously within 24 hours.

Thirteen additional patients with chronic decompensation of the right heart received alternately for 8 to 12 days 3 Gm. of ammonium chloride daily combined with 1 cc. of mercaptomerin (Thiomerin) once a week, and 500 mg. of chlorothiazide given twice a day. The diuretic effect obtained by these 2 methods of treatment was about the same, but resistance to chlorothiazide did not develop and chlorothiazide did not cause any side-effects. At present chlorothiazide is considered the diuretic of choice for the treatment of cardiac edema, because it can be administered orally, its diuretic action is satisfactory, and undesirable side-effects occur only rarely.

Clinical Experiences with the Anticoagulant Warfarin Sodium ("Coumadin Sodium"). R. R. Porter, D. Richardson and H. Page Mauck Jr. Virginia M. Month. 85:465-471 (Sept.) 1958 [Richmond].

The authors report a study on 80 patients with various thromboembolic disorders who have been treated with warfarin (Coumadin) sodium during the last 2 years at the McGuire Veterans Administration Hospital and the Medical College of Virginia Hospital in Richmond. The initial "priming" dose of Coumadin varied from 25 to 75 mg. as a single dose and from 50 to 100 mg. as a double dose administered orally, and from 50 to 60 mg. as a single dose administered intravenously. The sensitivity of patients to Coumadin varies from individual to individual, but it is fairly constant in the same patient. It would appear that a standard dose of 50 to 60 mg. will be suitable in the vast majority of patients weighing between 60 and 80 kg. (133 and 177 lb.) and having initial prothrombin activities of from 60 to 100%. If the patient is unusually heavy or obese, the dose can be increased to 75 mg. The dose should be reduced for patients weighing less than 60 kg. if the initial prothrombin time is 50% or less and if heparin in significant amounts (more than 300 mg. intramuscularly or 150 mg. intravenously daily) is given concomitantly to achieve some measure of anticoagulation during the latent period, i. e., from the time of administration of Coumadin and the onset of therapeutic effects.

The fairly rapid and consistant hypoprothrombinemic effect of Coumadin as measured by the Quick one-stage method confirms the findings as previously reported by other authors. After the initial latent period of from 12 to 18 hours, there is a rapid decline in prothrombin activity, with therapeutic levels attained in 24 to 36 hours after administration. Within the dose range of 50 to 75 mg. there was little difference in the achievement of a therapeutic effect in this 24-to-36-hour period, regardless of the patients' weight. After initial and prompt anticoagulation effect with Coumadin, maintenance therapy can be instituted. The response to the initial dose will be an indication of the patients' sensitivity to Coumadin and will serve as a guide for subsequent maintenance therapy. After 2 or 3 days of adjustment a smooth maintenance is usually achieved on relatively constant dosage, depending on the therapeutic response. Small daily doses achieve smoother control than intermittent larger doses. Coumadin is free of toxic side-reactions, the only adverse effects being its pharmacological action leading to excessive hypoprothrombinemia from overdosage. This latter is readily counteracted by the administration of a single dose of 50 mg. of vitamin K_1. Coumadin appears to be superior to all other hypoprothrombinemia-inducing agents currently available and seems to be the drug of choice for anticoagulant therapy in thromboembolic disorders.

Treatment of Intermittent Claudication with Vitamin E. P. D. Livingstone and C. Jones. Lancet 2:602-604 (Sept. 20) 1958 [London].

The authors report on 40 nondiabetic male patients with obliterative vascular disease who complained of intermittent claudication. Symptoms had been present for at least 5 years, and in all the patients the pain was felt in the calf muscles. Twenty of the 40 patients were treated with vitamin E and 20 were given placebos. The average age of the patients who received vitamin E was 55.9 years and that of the control group, 57 years. There were 3 patients, aged 40 to 50 years, in each group. A full general examination, with particular attention to the lower limbs, was carried out. Bilateral femoral arteriography showed pronounced arteriosclerotic changes and occlusion. Exercise tolerance tests were performed by climbing up and down a series of 2 steps, 18 in. high, until pain made the patient stop. The results of these tests were evaluated by the patients' own assessment and by the improvement in the average number of circuits (climbing up and down the steps) in the course of the treatment. Treatment was discontinued in 3 patients of each group. Four of the 17 patients who remained in the group treated with vitamin E did not respond at all to treatment. The remaining 13 patients showed much improvement; 7 were able to continue walking indefinitely at a slightly slower pace than usual, 4 were able to walk any distance of up to half a mile and do their full work, and 2

showed slight, but definite, improvement judged by the increase in the number of circuits and steps, and the patients were quite certain that they were more active than they had been and that the pain was less severe. Two of the patients in the control group recovered sufficiently to walk a useful distance. One of these, for no apparent reason, made a complete recovery after suffering from severe claudication for many years. All the other patients in this group derived no appreciable symptomatic relief. Six months after the end of the trial, none of the treated patients, who had improved, had deteriorated; and 3 patients in the control group, who had been transferred to vitamin E therapy at the end of the trial, reported some improvement.

Observations on Peroral Therapy for Diabetes. E. Ikkala and W. J. Kaipainen. Ann. med. int. Fenniae **47**:63-73 (No. 2) 1958 (In English) [Helsinki].

Peroral therapy was adopted at the end of 1955 in the outpatient department of the University of Helsinki for 22% of the 675 patients with diabetes who attended the clinic regularly. Peroral treatment with BZ 55 (Alentin) or D 860 (Diabuton) was given to 147 diabetics. In selecting patients for this therapy, mostly older obese diabetics were chosen. The treatment was not given to juvenile diabetics, to patients using large quantities of insulin or those receiving this drug for more than 10 years, and to patients predisposed to ketonuria. Of the 147 diabetics, 27% were fresh cases (no dietary or insulin therapy for more than a month), 43% had been earlier on dietary therapy, and 30% had been earlier on insulin therapy. Seventy-nine per cent of the perorally treated group were women. More than half of the cases were followed up for over a year.

A distinctly better blood sugar equilibrium was generally established with the peroral drugs in the group of fresh cases (40 patients) and in the 63 patients earlier on dietary therapy. Of 459 insulin-treated patients under observation, a switch to peroral therapy was made in the case of 61; in 44 patients the peroral drugs could be substituted for insulin, but in 9 (some of these did not meet the requirements for selection) they were ineffective, and in 8 they were withdrawn for other reasons. Insulin therapy was thus replaced by peroral therapy in 9.6% of the cases.

A weight gain, especially among diabetics earlier on dietary therapy, was observed in spite of a warning to the patients that they should follow previously issued dietary instructions. Of 33 patients who were started on peroral therapy but had to discontinue it, 6 were clearly outside the category for selection; the therapy was considered unnecessary for another 6 patients and was discontinued for 10 at their own request, although no detrimental side-effects were demonstrable. The peroral therapy had to be terminated because of ineffectiveness in 8 patients, who had shown all indications for successful treatment, and in 3 because of allergic reactions to BZ 55. Ineffectiveness of the peroral treatment usually became evident within a month of experimentation.

Effect of Chlorothiazide on Renal Electrolyte Excretion. U. V. Lassen and O. Munck. Ugesk. læger **120**:1112-1115 (Aug. 21) 1958 (In Danish) [Copenhagen].

A single dose of chlorothiazide administered to normal persons was followed by greatly increased secretion of sodium and chloride ions and some increase in bicarbonate and ammoniac excretion. The creatinin clearance was not affected. If chlorothiazide is given intermittently on good indication, electrolyte disturbance will rarely occur, at all events not in persons on a normal diet. Overdosage of chlorothiazide caused metabolic acidosis, hypokalemia, and hypochloremia.

Chlorothiazide Treatment of 10 Patients with Edema. C. Michelsen. Ugesk. læger **120**:1118-1121 (Aug. 21) 1958 (In Danish) [Copenhagen].

The results of chlorothiazide treatment in 11 patients with edema are discussed. Daily examinations of the serum and urine for values of potassium, sodium, bicarbonate, and chloride, determinations of the pH and pCO_2 of the blood, and diuresis were carried out; there was also regular control of the urine for protein, of serum uric acid and creatinin values, and of blood pressure and weight. In one patient treatment had to be discontinued because of hypokalemia. In 3 patients the treatment was without effect. The remaining 7 patients showed increased diuresis and increased excretion in the urine of sodium, potassium, and bicarbonate. In about half of the patients there was a tendency to a low serum potassium level. No essential shiftings in the acid-base conditions were seen in any case. Two patients were treated with chlorothiazide for a longer time.

Local Treatment of Bronchial Asthma with Hydrocortisone Powder. H. Herxheimer, M. K. McAllen and D. A. Williams. Brit. M. J. **2**:762-765 (Sept. 27) 1958 [London].

The authors report on 79 patients with chronic bronchial asthma who were treated by inhaling a capsule of micronized hydrocortisone snuff from a powder inhaler. A capsule, containing 15 mg. of hydrocortisone and 85 mg. of lactose, was placed in this inhaler; half of the contents were inhaled in the morning and half in the evening. Forty-five of the 79 patients served as their own controls; a few of the 45 were given hydrocortisone snuff for

2 weeks, followed by a similar period during which hydrocortisone snuff was not given; in most of the 45 patients the hydrocortisone snuff period was followed or preceded by an equal period of placebo snuff. A definite improvement in symptoms occurred in 33 of the 45 patients. This improvement was observed mainly in patients with a history of allergy and in those without hypersecretion. Improvement was seen to a much less extent in patients with the infective type of asthma than in those with the allergic type. Patients with "dry" asthma, i. e., those who never expectorated any mucus except during rare and short periods of upper respiratory infection, responded dramatically. These findings show that the result of topical treatment in any group of patients with asthma will mainly depend on the type of asthma involved. The hope that the topical treatment of bronchial asthma might replace steroid systemic therapy in most cases and might thus avoid the dangers of continuously given large systemic maintenance doses has not materialized; only a minority of patients appear to be benefited by corticoids given topically.

Bronchial Asthma and Chronic Bronchitis Treated with Hydrocortisone Acetate Inhalations. W. H. Helm and F. Heyworth. Brit. M. J. 2:765-768 (Sept. 27) 1958 [London].

Twenty-five male and 28 female patients, between the ages of 15 and 61 years, with asthma or wheezy bronchitis of at least one year's duration, whose condition had been severe enough to necessitate periods off work, were hospitalized and treated with antibiotics and routine antispasmodic drugs before receiving hydrocortisone inhalations. The patients inhaled fine hydrocortisone acetate powder from a "pabracort" inhaler, the powder being in capsules containing 15 mg. of hydrocortisone acetate and 75 mg. of lactose powder, both being ground fine to a mean particle size of 5 μ. The initial dose varied between 1 capsule 3 times a day and 1 capsule daily, given as half a capsule twice daily, according to the severity of the wheezing at the beginning of treatment. The dose was reduced to the minimum maintenance necessary as soon as improvement occurred. The usual maintenance dose was half a capsule twice daily. Treatment was stopped in patients with recurrent asthma, once the attack had been relieved for a week, and they were provided with capsules and instructed to restart at the onset of symptoms in a dose of between 1 and 3 capsules daily according to the severity of the attack. Patients who had failed to make any definite improvement during 2 weeks' treatment with inhalations were assessed as failures, and the treatment was stopped.

Of the 53 patients, 43 (81%) improved on hydrocortisone inhalations, whereas 10 (19%) were not improved. Of the 43 patients who improved, 13 (30%) relapsed after periods of 1 to 11 months, whereas 30 (70%) maintained the improvement for periods varying between 2 months and 2 years. Best results were obtained in patients with recurrent acute asthma without significant bronchial infection, whereas the results in patients with wheezy bronchitis were disappointing. There were no definite complications, but one man had mild dyspepsia for a few weeks, which may have been due to the hydrocortisone. Several patients put on weight, which was probably due partly to improved health and partly to the effects of hydrocortisone absorption.

The inhalations of fine-particle hydrocortisone acetate powder thus were found to be an effective form of treatment in many patients with bronchial asthma. There is a strong tendency to relapse if the treatment has to be maintained, but prolonged benefit may continue if the inhalations can be used intermittently for recurrent attacks of asthma. Although the treatment may be successful in status asthmaticus, it is probably less effective in this condition than intravenous or oral administration of corticosteroid drugs, and its use is not recommended if the patient is dangerously ill. A considerable portion of the "inhaled" hydrocortisone is probably absorbed, but the dosage is low compared with that used in oral therapy with a corticosteroid, and the chance of toxic effect is, therefore, much less. The optimum dosage is uncertain, but it probably varies from patient to patient. Little or no benefit is likely to be obtained from this form of treatment in patients with established chronic bronchitis.

Inhalation of Hydrocortisone Acetate for Bronchial Asthma: A Short-Term Controlled Trial. W. H. Helm and F. Heyworth. Brit. M. J. 2:768-769 (Sept. 27) 1958 [London].

A short-term controlled trial of inhalations of hydrocortisone acetate in fine-particle powder was carried out by the "double-blind" method during 38 trial periods in 14 men and 12 women with bronchial asthma of at least one year's duration. Of the 26 patients, 17 were treated by inhalations of hydrocortisone powder; 14 of these were improved, and 3 were not improved. Of the remaining 9 patients treated by inhalations of a placebo powder, 3 were improved and 6 were not improved. Thus, the number of patients improved in the hydrocortisone-treated group as compared with the placebo-treated group was at a statistically significant level. Hydrocortisone powder inhalations, therefore, are an effective form of short-term treatment in some patients with bronchial asthma.

Nature and Treatment of Septic Shock. W. A. Altemeier and W. R. Cole. A. M. A. Arch. Surg. 77:498-507 (Oct.) 1958 [Chicago].

The survival of 16 patients in a series of 41 with septic shock is indicative of the effectiveness of the basic principles of treatment which have been evolved. The importance of treatment and an early recognition of septic shock cannot be overemphasized. Delay in diagnosis and failure to recognize the septic cause of the circulatory collapse when the process becomes terminal or irreversible are chief factors responsible for failure of therapy. Early diagnosis and treatment will be facilitated if the significance of the characteristic sharp curves of rising temperature, pulse rate, and white blood cell count and the coincident inverted curve of falling arterial pressure and urinary excretion are kept in mind. The fact that only 25% of these patients demonstrated any evidence of hemoconcentration has supported the belief that large amounts of fluid replacement are not indicated and that they may be harmful in producing pulmonary edema if used in a vain effort to restore the blood pressure.

The intravenous infusion of arterenol in 5% dextrose in water has appeared to be particularly useful when regulated to maintain a systolic blood pressure above 80 mm. Hg and a urinary output of 25 cc. or more per hour. By this method it has been possible to maintain urinary function until the infection has been brought under control and to permit survival of the kidneys. Arterenol was administered for periods up to 144 hours to 15 of the 16 patients who survived. It was infused through indwelling polyethylene tubing, thus preventing local cutaneous gangrene. Large doses of intravenously administered antibiotics seemed efficacious in controlling the infection, but 2 to 7 or more days were required for this effect. This delay emphasized the importance of adequate supportive treatment to extend life until the antibiotic effect could be obtained. When arterenol was found to be inadequate, hydrocortisone in doses up to 100 mg. was given to 3 patients; without it, it is doubtful whether any of these patients would have survived. Eleven of the 16 surviving patients received blood or plasma or both, the amounts varying from 500 to 4,500 cc. Thirteen patients were given oxygen therapy over periods of 24 to 168 hours. It is generally better to treat patients with a severe uncontrolled infection conservatively, but surgical intervention may be necessary in those manifesting sudden vascular collapse. It takes critical judgment to determine which patients with septic shock require operation and the time when this is feasible.

PATHOLOGY

Failure to Prove Identity of Tumor Cells in the Peripheral Blood. F. W. Taylor and F. Vellios. Surgery 44:453-456 (Sept.) 1958 [St. Louis].

The concept that there may be occasional showers of cancer cells in the peripheral blood of cancer patients is not new, and interest in this problem was revived by a monograph published by Engell in 1955. The authors felt that one means of definitely establishing the identity of such cells would be to reinject the suspected cells in the hope of producing a metastasis. Four patients were studied who were in the terminal phase of neoplastic disease. All had carcinoma (of lung, stomach, or colon) with widespread extension; "tumor cells" were demonstrated in the peripheral blood of each. The patients died at intervals of 2 to 7 months after the investigation.

In carrying out the investigation, blood was drawn from the antecubital vein into a heparin solution or was taken from the femoral artery. The blood was then spun for 15 minutes at 1,500 rpm, so that a buffy coat could be isolated. This layer was mixed with a small quantity of isotonic sodium chloride solution to make approximately 2 ml. This mixture contained most of the suspicious abnormal cells present in a 50-to-80-ml. sample of the patient's peripheral blood. Twelve such samples were withdrawn from the 4 patients. The buffy coat mixture was reinjected into the patient from whom the sample was taken, usually into a marked area of subcutaneous fat or muscle, but on some occasions it was given intradermally as well. The injection resulted in a local lump, which was observed to diminish in size until no palpable nodule was present 2 months after injection. After death the tissues at the injection site showed little or no gross abnormality. Under microscopic examination there were a little fibrosis, hemosiderin, foreign-body giant cells, and occasionally nuclear fragments. There was, however, never any evidence of tumor cells at the site of injection. No secondary tumor growth resulted.

The authors feel that this failure to reproduce tumor growth from suspected tumor cells in the peripheral blood stream neither proves nor disproves them to be circulating cancer cells. Reasons suggested why these cells might not reproduce a secondary lesion include that the number injected was probably comparatively small and that they were injected with huge numbers of leukocytes. As this mass of leukocytes undergoes degeneration, various ferments are liberated which are highly detrimental and lytic to all cell protoplasm. The tumor cells might well be lysed as a result. Furthermore, the host must have the ability to eliminate stray tumor cells, for otherwise metastases would be unlimited. The elected sites of injection (skin, subcutaneous fat, and muscle) may not have been ideal.

What happens to all these circulating "tumor cells"? The authors never identified or recognized any cells being phagocytized or undergoing degenerative changes. They believe these must be cancer cells, but the final proof is lacking.

"Insulitis" in Early Juvenile Diabetes. P. M. LeCompte. A. M. A. Arch. Path. **66**:450-457 (Oct.) 1958 [Chicago].

The author reports on 2 infants, a boy and a girl, aged 11 months, a 9½-year-old boy, and a 17-year-old boy with diabetes mellitus who died within a short time after onset. Autopsy was performed on the 4 patients, and cellular infiltration, usually lymphocytic, of the islands of Langerhans was observed on microscopic examination of the pancreas in all of them. Some of the features of this rare but possibly significant lesion, described previously by other workers, were observed again, such as the variable appearance of the islands (of 2 islands of Langerhans in one patient, one appeared to be essentially normal, while the other showed lymphocytic infiltration); the narrow ribbon-like cords of cells with scanty cytoplasm and darkly stained nuclei, which are apparently alpha-cells and which probably are a manifestation of injury rather than of effective regeneration; the often peripheral distribution of the lymphocytes; and the occasional early fibrosis of an island. Hydropic change, the classical lesion of acute diabetes of recent onset, was seen in only 1 of the 4 patients but was also uncommon in the previously reported cases of "insulitis."

Cellular infiltration, usually lymphocytic, of the islands of Langerhans is observed most often in diabetes mellitus of acute onset and short duration in children. Its apparent rarity may be due in part to the fact that such acute cases come to autopsy only under exceptional circumstances. This "insulitis" may in a few instances be a response to actual invasion of the islands by an infectious agent, although this has not been demonstrated. It is more likely the aftermath of an injury which may differ from the injuries involved in the commonly recognized forms of experimental diabetes. It is probable that this injury in some way inhibits the regeneration of beta-cells.

Histochemical Proof of Organic Phosphate Poisoning. C. S. Petty, A. M. A. Arch. Path. **66**:458-463 (Oct.) 1958 [Chicago].

The author reports a case of fatal organic phosphate poisoning in a 23-year-old man who on the morning of illness and death had been cleaning an airplane which had been used 5 days previously for crop dusting with Systox, an insecticide concentrate containing 26.2% of O,O-diethyl-O-2-ethyl mercaptoethyl thiophosphate (Demeton), 2.3% related organic phosphates, and petroleum distillate. Since all organic phosphates combine more or less irreversibly with the cholinesterases of the body, the red blood cell cholinesterase activity was studied during the acute phase of the illness and on autopsy, and the enzyme activity at the myoneurol junction in skeletal muscle was studied on autopsy. The abnormally low antemortem red blood cell cholinesterase level indicated poisoning by one of the organic phosphates. The low postmortem red blood cell cholinesterase level, together with the results of the histochemical staining of the intercostal muscle which did not provide evidence of cholinesterase activity, gave proof of fatal poisoning due to exposure to toxic organic phosphates. In vitro studies with human muscle and both in vitro and in vivo studies with rat muscle showed that Systox is capable of depressing the cholinesterase level at motor end-plates.

Whipple's Disease—Observation on Systemic Involvement: I. Cytologic Observations. J. C. Sieracki. A. M. A. Arch. Path. **66**:464-467 (Oct.) 1958 [Chicago].

The author carried out cytological studies on autopsy specimens, including small intestine, mesenteric, axillary, inguinal, and peripheral lymph nodes, and various other tissues and organs, obtained from 7 patients who died of intestinal lipodystrophy (Whipple's disease). A widespread involvement of the tissues of all these patients was observed with cells which contained characteristic sickle-form, periodic acid-Schiff (P. A. S.)-positive cytoplasmic particles. These particles were found in mesothelial cells of the pleural, peritoneal, pericardial, and synovial lining cells. Their presence in a cell block of peritoneal fluid suggested the possibility of entertaining the diagnosis of Whipple's disease from such material. Smears stained according to Papanicolau technique left the characteristic particles unstained and showed the positive P. A. S. reaction when subsequently stained appropriately. Furthermore, the positive particles were diastase-resistant. In smears and imprints stained by the Romanovsky method, numerous vacuolated histiocytes were found. The nuclei of all histiocytes were similar in appearance. One group of these macrophages were the usual type of lipid-containing histiocyte "foam cells," with predominantly uniform-sized cytoplasmic vacuoles; another type, in which the apparent "vacuoles" were less distinct, varied in size and gave the cytoplasm a "moth-eaten" appearance. When these cytological preparations were subjected to the periodic acid-Schiff technique, these 2 varieties of histiocytes were again apparent. The histiocytes without lipid generally contained varying numbers of the sickle-form, positive-reacting particles. Less frequently, cells with uniform-sized vacuoles (foam cells) showed one or more positive sickle-form particles. This was particularly prominent in those

preparations containing giant cells. The presence in the peripheral lymph nodes of cells with the characteristic cytoplasmic particle allows the diagnosis of Whipple's disease to be made during life without recourse to laparotomy.

Cerebral Mucormycosis: Report of a Case. M. E. Smith, D. K. Burnham and M. B. Black. A. M. A. Arch. Path. **66**:468-473 (Oct.) 1958 [Chicago].

The authors report on a 38-year-old man with diabetes mellitus of 14 years' duration, who was admitted to hospital in coma. History showed that one week before admission he had sinusitis, with stuffiness in the nose and fever. At no time in his life had he had diabetic coma, and, although he was deeply comatose on admission, he did not have acidosis. There were marked proptosis of the right eye and edema of the right lid. He had difficulty in urinating. A clinical diagnosis of labile diabetes, subacute glomerulonephritis, and cavernous sinus thrombosis was made, and the patient received antibiotic therapy, intravenous fluids, and artificial respiration. He died 36 hours after admission.

Gross findings on autopsy consisted of hypertrophy of the heart, moderate coronary artery sclerosis, and edematous brain, with almost the entire right temporal lobe being replaced by clotted blood; a second hemorrhagic zone was near the midline of the cerebellar medulla on the right, extending into the upper pons. Both internal carotid arteries and the superior sagittal and right lateral venous sinuses contained thrombi. The cavernous sinuses also contained thrombus material. Microscopic examination revealed that both carotid arteries contained unorganized thrombus attached to the intima and tangled masses of broad branching nonseptate hyphae; the cavernous sinus contained small masses of thrombus and fungal hyphae, both free and invading nerves and fibrous fasciculi in the lumen. The walls of the cavernous sinus showed acute inflammatory reaction and hyphae. Hyphae were also observed in the submucosa of the sphenoid air sinus. An acute meningitis was confined to the area of the optic chiasm. A few hyphae lay inertly in the midbrain parenchyma above the chiasm, unassociated with inflammation. One bronchus was the site of an acute necrotizing ulcerating inflammation containing numerous hyphae. Other findings included advanced diabetic glomerulosclerosis, marked renal arteriosclerosis, bilateral chronic pyelonephritis, and multiple thromboses of small pulmonary arteries.

The true nature of the patient's disease was not discovered until the microscopic examination. Cultures for fungi were not made during life or at autopsy. The ethmoid sinuses and orbits were not investigated at autopsy. The evidence indicated that the infection arose in nose and paranasal sinuses and/or orbit and spread to the brain by way of the internal carotid arteries and cavernous sinuses. Proptosis and ophthalmoplegia were characteristic and apparently attributable to direct fungal invasion of the eye and retrobulbar space. In most cases collected from the literature, the mycotic infection was limited to the head. It is likely that in this patient the bronchial involvement was a separate primary focus, since there was clinical evidence of preceding orbital and sinus involvement. Characteristically there was total lack of inflammatory reaction to hyphae in some areas and a marked response in others.

Cerebral mucormycosis is a rare but distinctive entity, usually a rapidly fatal complication of diabetes mellitus. The case of this patient is a classical example. Since the 17 patients in the previously reported cases had rather stereotyped manifestations, more widespread knowledge of this condition should result in more frequent diagnoses during life and more thorough investigation at autopsy. Routine examination of paranasal sinuses in patients with diabetes mellitus coming to autopsy might help elucidate the pathogenesis.

Behavior of Leukocyte Sedimentation Rate in Tuberculous Disease and in Septic Infections. E. Lusvarghi, L. Bellesia and P. Mucci. Minerva med. **49**:2735-2737 (July 11) 1958 (In Italian) [Turin, Italy].

Leukocyte sedimentation rates, according to the technique of Storti, were investigated simultaneously in 2 groups of patients. One group consisted of 20 patients with various types of pulmonary tuberculosis. The other group consisted of 10 patients with acute and chronic types of bacterial sepsis. Erythrocyte sedimentation rates were recorded for control purposes. Leukocyte sedimentation rates were determined before and several times during the treatment until the clinical cure of the disease. In patients with pulmonary tuberculosis and with bacterial sepsis the latter rates were above normal values. There was a close correlation between the leukocyte sedimentation rates and the Katz formula levels at the onset or at the termination of the disease. The leukocyte sedimentation rates were elevated and the Katz formula levels were within limits only in 1 patient with active bilateral tuberculosis of the apex and in 3 patients with bacterial sepsis. An increased level of fibrinogen seemed to be responsible for an elevated leukocyte sedimentation rate, whereas qualitative and quantitative changes in albumin and globulin values apparently had no bearing on it. Increased leukocyte sedimentation rates in patients with pulmonary tuberculosis and with bacterial sepsis indicated a probable direct participation of the leukocytes in the defense of the organism. Study of the leukocyte sedimentation rate is a useful diagnostic aid to be used along with the erythrocyte sedimentation rate. It can clarify in differential diagnosis certain roentgenologic findings in the lung and distinguish pulmonary tuberculosis from malignant tumors.

BOOK REVIEWS

Chronic Bronchitis, Emphysema and Cor Pulmonale. By C. H. Stuart-Harris, M.D., F.R.C.P., Sir George Franklin Professor of Medicine of University of Sheffield, Sheffield, and T. Hanley, M.D., M.R.C.P., Lecturer in Medicine of University of Sheffield. Written in collaboration with Marjorie Clifton, M.D., Research Assistant to M.R.C. Group for Epidemiological Research on Respiratory Diseases, London, Margaret M. Platts, M.D., B.Sc., M.R.C.P., J. D. S. Hammond, M.B., Ch.B., M.R.C.P., and W. Whitaker, M.D., M.R.C.P. Cloth. $8.50. Pp. 245, with 61 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1957.

The authors are to be commended on their choice of subject. Chronic bronchitis and emphysema are ubiquitous and imply serious consequences which more than justify bringing recent data to the attention of the medical profession. Each chapter carries worthwhile material. The authors recognize the smallness of the number of patients observed, which may detract somewhat from the weight of evidence presented. Even so, their focus on the salient features of these diseases, objectivity in observation, and sound logic in interpretation render the text of great value. The sincere dedication and praiseworthy thoroughness of the authors is impressive. Their preferential definition of chronic bronchitis is serviceable although it may not coincide with the concepts of other experts in this field. The clinical findings of chronic bronchitis are portrayed in an excellent manner. Various objective signs and findings on physical and x-ray examination are presented briefly but competently. The fallibility of some of the physical findings is well emphasized. The relation of infection to chronic bronchitis and emphysema is discussed concisely but adequately. Pathological and clinical aspects of emphysema are well described, although it is difficult to condone the omission of one of the cardinal pathological substrates of this disease, namely, destructive changes in the elastic elements of the lung.

There is a fine, practical section on pulmonary function studies. Nearly 60 pages deal with chronic cor pulmonale. Its incidence, clinical characteristics, and pathological physiology are skillfully covered. Current knowledge of pulmonary arterial blood pressure, cardiac output, oxygen-carrying capacity of the blood, and other related facets of the subject are assayed in lucid, easily readable fashion. The chapter on treatment is logical and methodical. Emphasis on the use of bronchospasmolytic drugs deserves special credit. Also commendable is the authors' cautious attitude toward the administration of narcotics as cough sedatives, and to use of oxygen for the relief of dyspnea. At the same time, their dogmatic negativism is hardly justifiable concerning artificial pneumoperitoneum and the surgical treatment of emphysema. The chapter on the epidemiology and pathogenesis of chronic bronchitis is written with critical analysis and is solidly documented. It contains tables and graphs that facilitate clear comprehension of the subject matter. The roentgenograms and photographs of gross specimens and histological preparations are of high quality. The case reports are of great didactic value. The references at the end of each chapter are well selected and up to date, and the index covers all essential items. Blank pages at the end of the book invite pertinent notes. This volume is likely to become a favorite with all those interested in diseases of the chest.

Bacterial and Mycotic Infections of Man. Edited by René J. Dubos, Ph.D. Aided by grant from National Foundation. Third edition. Cloth. $8.50. Pp. 820, with 116 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada; Pitman Medical Publishing Company, Ltd., 45 New Oxford St., London, W. C. 1, England, 1958.

This edition of a classic textbook combines bacteriology with practical clinical application. While the essential format of the previous editions remain the same, the book has been completely rewritten to present changing concepts concerning microbial diseases. A previous criticism of the book, that it lacked continuity, has been vitiated by its reorganization. New chapters include "The Evolution and Ecology of Microbial Diseases" and "Chemotherapy of Microbial Diseases." The first of the new chapters contains many points of view not necessarily shared by other contributors to the text, but these speculative concepts of infection versus disease (why do pathogens so often fail to cause disease after they have become established in the tissues?) provide a broad background to the understanding of disease determinants. Much praise must be given for the valuable material on antigen-antibiotic reactions and anaphylaxis. The chapter on the principles of sterilization should be valuable to every physician and his office staff.

While the general emphasis is on prevention and the potential disease state (host-parasite relationship), there is much information on the principles of chemotherapy as applied to clinical practice, including complete discussions on the individual

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

chemotherapeutic agents. Other chapters contain discussions on human blood groups, epidemiology, principles and practice of diagnostic medical bacteriology, and specific pathogenic groups of bacteria and fungi. Because of financial support from the National Foundation, the book sells for a remarkably low price, especially considering the style of presentation (profuse tables, diagrams, and illustrations; excellent type and paper; complete index; and a careful, comprehensive bibliography) along with its content and its authors of exceptional reliability. The book is highly recommended to students and clinicians who deal with infectious disease.

A History of the Department of Internal Medicine, State University of Iowa College of Medicine, 1870-1958. By Walter L. Bierring, M.D. With introduction by William B. Bean, M.D. Cloth. $3.50. Pp. 116, with illustrations. State University of Iowa, Iowa City, 1958.

This little volume is of special interest because it has been prepared by Dr. Walter L. Bierring, whose life span began almost on the birthday of the College of Medicine of the State University of Iowa. It contains an interesting introductory chapter outlining the history of the College of Medicine and a brief one on the history of the department of internal medicine. The main body of the volume, however, is devoted to biographical and autobiographical résumés of the eight persons who have occupied the chair of the department originally called theory and practice of medicine, which today is the department of internal medicine. These brief sketches offer an interesting portrayal of the progress of medicine during this 90-year period. Those concerned with the management and utilization of the modern teaching hospital should find the description of the Rules and Regulations for the Government of the University Hospital in 1898-1899 of particular interest.

Cerebral Vascular Disease: Transactions of the Second Conference Held Under the Auspices of the American Heart Association, Princeton, New Jersey; January 16-18, 1957. Irving S. Wright, chairman. Clark H. Millikan, editor. Including classification and outline of cerebrovascular diseases. Report by ad hoc Committee established by Advisory Council for National Institute of Neurological Diseases and Blindness, Public Health Service. Cloth. $4. Pp. 224. Published for American Heart Association by Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This book covers the problems of nomenclature and has, as an appendix, a classification and outline of cerebrovascular diseases prepared by a committee under the chairmanship of Dr. Millikan which should go a long way toward crystallizing thinking in this important area. The rest of the monograph deals with specific aspects of the subject presented by authorities in the field, together with the discussion which followed each presentation. Thus, Drs. R. D. Adams and H. Fang covered the anatomy and pathology of the cerebral blood vessels; Dr. G. Nylin discussed cerebral blood flow and blood pool; Dr. A. C. Corcoran, the interrelation of hypertension and cerebral vascular disease; Dr. J. P. Whisnant, experimental cerebral vascular disorders; Dr. C. M. Fisher, intermittent cerebral ischemia; Dr. J. Stamler, the cause and therapy of atherosclerosis; Dr. E. McDevitt, anticoagulant therapy; Dr. E. Cliffton, experiments on enzymes in treating thrombosis and embolism; Dr. E. H. Botterell, surgery of intracranial aneurysmal hemorrhage; and Dr. P. Lee, rehabilitation. The gaps in our knowledge are stressed. No one interested in cardiovascular diseases can afford to neglect reading this monograph carefully. It should go a long way in bringing to the fore a much neglected aspect of medicine. Dr. I. Wright, who was responsible for this symposium, as well as the first one, deserves much praise, as do the persons and agencies who supported it. They and the participants have rendered a great service to the medical profession.

Clinical Endocrinology. By Karl E. Paschkis, M.D., Associate Professor of Medicine, Jefferson Medical College, Philadelphia, Abraham E. Rakoff, M.D., Clinical Professor of Obstetrics and Gynecologic Endocrinology, Jefferson Medical College, and Abraham Cantarow, M.D., Professor of Biochemistry, Jefferson Medical College. Second edition. Cloth. $18. Pp. 941, with 274 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This book is divided into sections on the anterior pituitary, posterior pituitary, thyroid, adrenal cortex, adrenal medulla, ovaries, placenta, testes, pancreas, parathyroids, obesity, and methods and materials. The chapters in each section deal with the embryology, anatomy, physiology, and disorders of the various glands. This book reflects the increase in endocrine knowledge since its first edition, particularly in the fields of thyroid and adrenal physiology, pathology, and therapy. The authors have done an extensive and commendable job of revising and, in some instances, rewriting chapters. They discuss in common-sense terms the male climacteric, the existence of which is denied by some authors. The term may be unfortunate, but few experienced observers will deny that some aging men exhibit the clinical findings mentioned by these authors. Their condition is greatly alleviated by the administration of androgens.

This excellent reference book suffers from the faults or weaknesses of all books in this field. There is an overemphasis on the value of laboratory findings and too little value attached to a careful history and physical examination. It also deals primarily with severe, far-advanced, "typical" cases. It is doubtful if this could be otherwise since the diagnosis is doubtful enough, in some instances, even in such cases, but disorders do have a beginning, a mild stage, before they become typical. These are seen not by endocrinologists, as a rule, but by general practitioners, surgeons, and in-

ternists. Such patients seldom have the time, means, or inclination to go through with a lot of expensive tests which at best may not be conclusive. Hyperfunction of the pituitary's eosinophilic cells is discussed as acromegaly. Gigantism is merely mentioned and yet in many cases it is preventable. In 1948 in a postgraduate course in endocrinology, irradiation of the pituitary was described as a method of preventing it. This mode had been used for 15 or 20 years at that time, in over 300 patients. The procedure has been in use for at least 25 years. Its discussion here would have been helpful. The authors would have done a great service to the American public and to the medical profession if they had included a chapter pointing out some of the signs and symptoms of endocrine disorders that could be elicited by a careful history and physical examination. Too often private practitioners are, by circumstances beyond their control, compelled to rely on the history and physical examination plus a therapeutic test. The more help we can give such men—and that means most physicians—the greater service we render the public and the profession. Incidentally, after the most extensive battery of laboratory tests the diagnosis can, in some cases, be settled only by a therapeutic test. This book should nonetheless be a valuable addition to any physician's library.

Congenital Anomalies of the Hand and Their Surgical Treatment. By Arthur Joseph Barsky, M.D., D.D.S., Professor of Clinical Surgery, Albert Einstein College of Medicine, New York City. Publication number 311, American Lecture Series, monograph in Bannerstone Division of American Lecture in Orthopaedic Surgery. Edited by Charles Weer Goff, M.D., Associate Clinical Professor of Orthopaedic Surgery, Yale University School of Medicine, New Haven, Conn. Cloth, $5.75. Pp. 165, with 77 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This excellent monograph is amply illustrated with roentgenograms and photographs of all deformities. Of particular value are the line drawings indicating the location of skin incisions in the operative repair of web fingers, floating thumb, lobster-claw hand, and other deformities. The work is based on a large personal series of 165 cases. It is well organized and has excellent chapters on incidence, cause, and various genetic, environmental, chemical, and endocrine factors. The effect of irradiation is briefly discussed, but, above all, the author has emphasized that heredity plays the greatest role in handing down defects to the germ plasm of the embryo. The bibliography is extensive and should be of great value. Credit is given to earlier authors for their pioneer work. The monograph is highly technical. It is a necessity in the library of the plastic surgeon and the orthopedist, but it is a little above the level of the medical student and the resident. To them it should be valuable as a reference book.

The Planning of International Meetings. Handbook issued by Council for International Organizations of Medical Sciences established under joint auspices of UNESCO and WHO. Paper. $2.50. Pp. 113. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada; published in French by Masson & Cie., 120 boulevard Saint-Germain, Paris 6e, France, 1957.

Those who have attempted to plan international meetings know the problems that can arise when men and women from various parts of the world attempt to meet on a common medical ground. While the spirit and the knowledge may have much in common, procedure can vary tremendously and is often an unnecessary source of irritation, particularly if improper planning is evident. This booklet is an attempt to provide guidance for planning and is worthy of careful study by those who are interested in the planning of such meetings, as well as by those who merely hope to attend but would like to get the most out of such sessions.

Manual of Medical Emergencies. By Stuart C. Cullen, M.D., Professor of Surgery; Chairman, Division of Anesthesiology, State University of Iowa College of Medicine, Iowa City, and E. G. Gross, M.D., Professor and Head of Department of Pharmacology, State University of Iowa College of Medicine. Third edition. Cloth, $5.75. Pp. 302, with 41 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This handy pocket-size book provides information without wasted details on many common problems that confront the practitioner. It is not as comprehensive as many textbooks are, but apparently it is not intended to be. Rather, it is to be used for quick reference. In this respect, interns and general practitioners may find it of greater value than others. There may be some forms of treatment, particularly with the newer drugs, that would be found missing, but this is the hazard associated with writing any medical book. Furthermore, there may be a dispute about treatment (such as the recommendation that a snakebite wound should be incised), but such criticisms do not detract from its usefulness.

The Early Diagnosis of the Acute Abdomen. By Sir Zachary Cope, B.A., M.D., M.S. Eleventh edition. Cloth, $4.50. Pp. 188, with illustrations. Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England; 114 Fifth Ave., New York 11; Amen House, 480 University Ave., Toronto 2, Canada, 1957.

This popular book has gone through sufficient editions to justify its broad acceptance. It is practical, helpful, and easily understood. Unfortunately, there is an appearance of crowding of type on the pages so that it is not easy to read, but for those who desire a ready reference source, to which they can go for a subject or a symptom without attempting to cover a system or the body as a whole, this book should be found practical because of the directness with which the author discusses the problem.

chemotherapeutic agents. Other chapters contain discussions on human blood groups, epidemiology, principles and practice of diagnostic medical bacteriology, and specific pathogenic groups of bacteria and fungi. Because of financial support from the National Foundation, the book sells for a remarkably low price, especially considering the style of presentation (profuse tables, diagrams, and illustrations; excellent type and paper; complete index; and a careful, comprehensive bibliography) along with its content and its authors of exceptional reliability. The book is highly recommended to students and clinicians who deal with infectious disease.

A History of the Department of Internal Medicine, State University of Iowa College of Medicine, 1870-1958. By Walter L. Bierring, M.D. With introduction by William B. Bean, M.D. Cloth. $3.50. Pp. 116, with illustrations. State University of Iowa, Iowa City, 1958.

This little volume is of special interest because it has been prepared by Dr. Walter L. Bierring, whose life span began almost on the birthday of the College of Medicine of the State University of Iowa. It contains an interesting introductory chapter outlining the history of the College of Medicine and a brief one on the history of the department of internal medicine. The main body of the volume, however, is devoted to biographical and autobiographical résumés of the eight persons who have occupied the chair of the department originally called theory and practice of medicine, which today is the department of internal medicine. These brief sketches offer an interesting portrayal of the progress of medicine during this 90-year period. Those concerned with the management and utilization of the modern teaching hospital should find the description of the Rules and Regulations for the Government of the University Hospital in 1898-1899 of particular interest.

Cerebral Vascular Disease: Transactions of the Second Conference Held Under the Auspices of the American Heart Association, Princeton, New Jersey; January 16-18, 1957. Irving S. Wright, chairman. Clark H. Millikan, editor. Including classification and outline of cerebrovascular diseases. Report by ad hoc Committee established by Advisory Council for National Institute of Neurological Diseases and Blindness, Public Health Service. Cloth. $4. Pp. 224. Published for American Heart Association by Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This book covers the problems of nomenclature and has, as an appendix, a classification and outline of cerebrovascular diseases prepared by a committee under the chairmanship of Dr. Millikan which should go a long way toward crystallizing thinking in this important area. The rest of the monograph deals with specific aspects of the subject presented by authorities in the field, together with the discussion which followed each presentation. Thus, Drs. R. D. Adams and H. Fang covered the anatomy and pathology of the cerebral blood vessels; Dr. G. Nylin discussed cerebral blood flow and blood pool; Dr. A. C. Corcoran, the interrelation of hypertension and cerebral vascular disease; Dr. J. P. Whisnant, experimental cerebral vascular disorders; Dr. C. M. Fisher, intermittent cerebral ischemia; Dr. J. Stamler, the cause and therapy of atherosclerosis; Dr. E. McDevitt, anticoagulant therapy; Dr. E. Cliffton, experiments on enzymes in treating thrombosis and embolism; Dr. E. H. Botterell, surgery of intracranial aneurysmal hemorrhage; and Dr. P. Lee, rehabilitation. The gaps in our knowledge are stressed. No one interested in cardiovascular diseases can afford to neglect reading this monograph carefully. It should go a long way in bringing to the fore a much neglected aspect of medicine. Dr. I. Wright, who was responsible for this symposium, as well as the first one, deserves much praise, as do the persons and agencies who supported it. They and the participants have rendered a great service to the medical profession.

Clinical Endocrinology. By Karl E. Paschkis, M.D., Associate Professor of Medicine, Jefferson Medical College, Philadelphia, Abraham E. Rakoff, M.D., Clinical Professor of Obstetrics and Gynecologic Endocrinology, Jefferson Medical College, and Abraham Cantarow, M.D., Professor of Biochemistry, Jefferson Medical College. Second edition. Cloth. $18. Pp. 941, with 274 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This book is divided into sections on the anterior pituitary, posterior pituitary, thyroid, adrenal cortex, adrenal medulla, ovaries, placenta, testes, pancreas, parathyroids, obesity, and methods and materials. The chapters in each section deal with the embryology, anatomy, physiology, and disorders of the various glands. This book reflects the increase in endocrine knowledge since its first edition, particularly in the fields of thyroid and adrenal physiology, pathology, and therapy. The authors have done an extensive and commendable job of revising and, in some instances, rewriting chapters. They discuss in common-sense terms the male climacteric, the existence of which is denied by some authors. The term may be unfortunate, but few experienced observers will deny that some aging men exhibit the clinical findings mentioned by these authors. Their condition is greatly alleviated by the administration of androgens.

This excellent reference book suffers from the faults or weaknesses of all books in this field. There is an overemphasis on the value of laboratory findings and too little value attached to a careful history and physical examination. It also deals primarily with severe, far-advanced, "typical" cases. It is doubtful if this could be otherwise since the diagnosis is doubtful enough, in some instances, even in such cases, but disorders do have a beginning, a mild stage, before they become typical. These are seen not by endocrinologists, as a rule, but by general practitioners, surgeons, and in-

ternists. Such patients seldom have the time, means, or inclination to go through with a lot of expensive tests which at best may not be conclusive. Hyperfunction of the pituitary's eosinophilic cells is discussed as acromegaly. Gigantism is merely mentioned and yet in many cases it is preventable. In 1948 in a postgraduate course in endocrinology, irradiation of the pituitary was described as a method of preventing it. This mode had been used for 15 or 20 years at that time, in over 300 patients. The procedure has been in use for at least 25 years. Its discussion here would have been helpful. The authors would have done a great service to the American public and to the medical profession if they had included a chapter pointing out some of the signs and symptoms of endocrine disorders that could be elicited by a careful history and physical examination. Too often private practitioners are, by circumstances beyond their control, compelled to rely on the history and physical examination plus a therapeutic test. The more help we can give such men—and that means most physicians—the greater service we render the public and the profession. Incidentally, after the most extensive battery of laboratory tests the diagnosis can, in some cases, be settled only by a therapeutic test. This book should nonetheless be a valuable addition to any physician's library.

Congenital Anomalies of the Hand and Their Surgical Treatment. By Arthur Joseph Barsky, M.D., D.D.S., Professor of Clinical Surgery, Albert Einstein College of Medicine, New York City. Publication number 311, American Lecture Series, monograph in Bannerstone Division of American Lecture in Orthopaedic Surgery. Edited by Charles Weer Goff, M.D., Associate Clinical Professor of Orthopaedic Surgery, Yale University School of Medicine, New Haven, Conn. Cloth. $5.75. Pp. 165, with 77 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This excellent monograph is amply illustrated with roentgenograms and photographs of all deformities. Of particular value are the line drawings indicating the location of skin incisions in the operative repair of web fingers, floating thumb, lobster-claw hand, and other deformities. The work is based on a large personal series of 165 cases. It is well organized and has excellent chapters on incidence, cause, and various genetic, environmental, chemical, and endocrine factors. The effect of irradiation is briefly discussed, but, above all, the author has emphasized that heredity plays the greatest role in handing down defects to the germ plasm of the embryo. The bibliography is extensive and should be of great value. Credit is given to earlier authors for their pioneer work. The monograph is highly technical. It is a necessity in the library of the plastic surgeon and the orthopedist, but it is a little above the level of the medical student and the resident. To them it should be valuable as a reference book.

The Planning of International Meetings. Handbook issued by Council for International Organizations of Medical Sciences established under joint auspices of UNESCO and WHO. Paper. $2.50. Pp. 113. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada; published in French by Masson & Cie., 120 boulevard Saint-Germain, Paris 6e, France, 1957.

Those who have attempted to plan international meetings know the problems that can arise when men and women from various parts of the world attempt to meet on a common medical ground. While the spirit and the knowledge may have much in common, procedure can vary tremendously and is often an unnecessary source of irritation, particularly if improper planning is evident. This booklet is an attempt to provide guidance for planning and is worthy of careful study by those who are interested in the planning of such meetings, as well as by those who merely hope to attend but would like to get the most out of such sessions.

Manual of Medical Emergencies. By Stuart C. Cullen, M.D., Professor of Surgery; Chairman, Division of Anesthesiology, State University of Iowa College of Medicine, Iowa City, and E. G. Gross, M.D., Professor and Head of Department of Pharmacology, State University of Iowa College of Medicine. Third edition. Cloth. $5.75. Pp. 302, with 41 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This handy pocket-size book provides information without wasted details on many common problems that confront the practitioner. It is not as comprehensive as many textbooks are, but apparently it is not intended to be. Rather, it is to be used for quick reference. In this respect, interns and general practitioners may find it of greater value than others. There may be some forms of treatment, particularly with the newer drugs, that would be found missing, but this is the hazard associated with writing any medical book. Furthermore, there may be a dispute about treatment (such as the recommendation that a snakebite wound should be incised), but such criticisms do not detract from its usefulness.

The Early Diagnosis of the Acute Abdomen. By Sir Zachary Cope, B.A., M.D., M.S. Eleventh edition. Cloth. $4.50. Pp. 188, with illustrations. Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England; 114 Fifth Ave., New York 11; Amen House, 480 University Ave., Toronto 2, Canada, 1957.

This popular book has gone through sufficient editions to justify its broad acceptance. It is practical, helpful, and easily understood. Unfortunately, there is an appearance of crowding of type on the pages so that it is not easy to read, but for those who desire a ready reference source, to which they can go for a subject or a symptom without attempting to cover a system or the body as a whole, this book should be found practical because of the directness with which the author discusses the problem.

QUESTIONS AND ANSWERS

PREVENTING STAPHYLOCOCCUS INFECTIONS IN THE NURSERY

To the Editor:—*In an attempt to control contamination by staphylococci in a hospital nursery, is there any practical value in obtaining nose and throat cultures on newborn infants at the time of discharge on the third day?*

M.D., South Carolina.

Answer.—Nose and throat cultures taken at the time of the baby's discharge from the hospital on the third day give important evidence in preventing an epidemic in the nursery by detecting carriers. They are also important in controlling an epidemic already present by giving information which would aid in tracing the method of spread of staphylococci in the nursery. This information supplements more important data from nose and throat cultures on asymptomatic mothers, nurses, and other personnel and from cultures from skin, blood, stools, and urine of infants and mothers with clinical evidence of infection. The greatest value of routine nose and throat cultures at the time of discharge would be to the family physician or pediatrician who attends the infant in the home. Such information would enable the physician to administer the appropriate antibiotic to infants with positive cultures before the onset of symptoms. It is important, therefore, that culture reports be immediately available to the family physician or pediatrician, as well as to the house staff.

PTYALISM

To the Editor:—*A 30-year-old man has been suffering from hypersalivation (ptyalism) for about 15 years. No dietary or emotional basis can be found for this annoying condition which fills up his stomach with saliva, causing heaviness in the upper abdomen and nausea. No pathology can be found locally. Anticholinergic drugs, atropine, and local mouth irrigations do not give any degree of improvement. Please advise what can be done for relief.*

M.D., New York.

Answer.—The hypersalivation would not cause "heaviness in the upper abdomen and nausea." The hourly secretion of "resting" salivary glands equals 15 cc., and the total amount of saliva secreted daily varies from about 600 to about 1,500 cc. or more. It is unlikely that even a substantial amount of hypersalivation would be related to the nausea in this case. On the contrary, nausea itself is a powerful stimulus for the salivary glands and would, therefore, cause hypersalivation. Therefore, a search for the actual cause of the nausea is in order. For example, one should be certain not only that the gastrointestinal series shows normal findings but that a barium enema and gallbladder studies also show normal results. If no organic basis for the nausea can be found, simple abdominal distention with gas may be the explanation and can be treated by the administration of belladonna tincture, 0.6 cc. before meals and at bedtime, and pavatrine, 125 mg. after meals; by the avoidance of iced drinks and cold foods; and by the taking of a hot drink before each meal. The following diet may be of value:

One-half glass of orange juice, diluted with one-half glass of hot water, should be taken on arising. If stools are hard or infrequent, this same amount of orange juice and hot water should be taken before each meal. If stools are loose, the orange juice should be omitted until they are formed. For breakfast, the following foods may be chosen from: Any cooked fruit, fresh, dried, or canned, may be stewed or baked. If canned fruit is used, it should be brought to a boil and cooled before eating. Well-cooked oatmeal or cream of wheat may be used, with puffed wheat and puffed rice during the summer. Bacon should be broiled and eggs soft-boiled, poached, baked soft in a ramekin dish, or scrambled in the top of a double boiler. Toast, preferably melba toast, should be of white bread, with butter spread on as it is eaten. Tea, coffee, or milk may be used (not more than one cup of coffee daily). The noon and evening meals may be chosen from the following list of foods: raw oysters, broth, or creamed soups made from the vegetables which are allowed on the diet; any white fish, such as halibut or haddock, or hot boiled lobster (no mackerel, salmon, clams, or any oily fish; fish should be boiled, broiled, or baked); beef, lamb, chicken, or broiled liver or kidneys; turkey, duck, and partridge (no dressings or gravies; meats may be in any form except boiled or from the frying pan or deep fat); potato, rice, or macaroni once or twice daily; native (garden) lettuce and celery—if possible, twice a day; other vegetables as follows: string beans, asparagus, spinach, carrots, raw carrot sticks, peas, cauliflower, beets, squash, artichokes, eggplant (boiled or broiled, not fried or scalloped),

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

and mushrooms, not sautéed; and desserts as follows: jello, cooked fruit, soft puddings, American, cream, cottage, Gruyère, Port du Salut, or Swiss cheese, and sponge or angel cake. White bread, or very fine graham bread, should be used, preferably cut thin and toasted dry, with butter to be spread on as it is eaten.

REGIONAL ENTERITIS AND ABSORPTION

To the Editor:—*A woman, aged 32, developed ankle edema with some constant and persistent pain in the lower part of the abdomen after delivery of her last child. The abdomen is slightly distended. There are no palpable masses and no tenderness on palpation. Examination of the intestines showed the lower portion of the ileum to be thickened for about 24 in. The diagnosis was regional ileitis. At operation, about 3 ft. of ileum was removed, with some enlarged mesenteric glands. She received about 5 units of serum albumin (low salt) and was advised to be on a high-protein diet. From 1945 until 1956 she had repeated blood protein examinations at about six-month intervals. The serum albumin level has always been low, and 6-10 intravenous injections of serum albumin, 25 mg. units, have been given. She has had persistent diarrhea since the operation. Repeated x-rays of the intestines at about yearly intervals revealed some recurrence of the ileitis. In 1956, she developed ascites, for which repeated taps were done, with recurrence every six days. In June, 1957, she was given 10 units of serum albumin intravenously; all liver function tests gave normal findings, and hematology was the same as in 1945. Exploratory examination of the abdomen revealed some extension of the ileitis. Liver, adnexa, stomach, large intestines, and the rest of the abdominal viscera were normal, and no reason for the recurrent ascites could be found. After six weeks of hospitalization she was discharged with instructions to be on a low-sodium and high-protein diet. Since July, 1957, she has received about 30 units of a serum albumin. She has lost about 20 lb. (9.1 kg.) in weight. She is taking chlorothiazide, 500 mg. three times a day, and is on a sodium-free diet, but the ascites is worse than ever, her appetite is very poor, and diarrhea persists. Urine output is normal. The blood protein level is always low before the serum albumin administration and returns to normal after. At present, she is very weak and hardly able to move about (weight, 102 lb. [46.3 kg.]). Please discuss etiology and treatment.* *David Cohen, M.D., Philadelphia.*

Answer.—The description in this case is that of a rather extensive, advanced regional enteritis, with possibly more involvement than is visible to the naked eye. In some of these patients there is great interference with the processes of absorption. A deficiency state occurs, resembling that resulting from long-standing depletion of protein or withholding of protein. The etiology of regional enteritis is, of course, obscure. The symptom complex described in this patient's case resembles that occasionally seen in a patient with regional enteritis in which the lesions are roentgenographically rather limited yet in which changes throughout much of the small intestine occur. Some of these patients have responded to roentgen therapy (Bargen, *J. A. M. A.* **165**:2045-2047 [Dec. 21] 1957). A high protein intake should be maintained. Edema and ascites may well be associated with lack of protein absorption.

TERTIARY SYPHILIS AND YAWS

To the Editor:—*Is there a definite method of differentiating between tertiary syphilis and tertiary yaws (framboesia)? The modifications of the Wassermann test (Ide's, Kolmer's, and others) and the Treponema pallidum immobilization test both may give positive results in either disease. What is the present treatment of choice in yaws? Has broad-spectrum antibiotic therapy given lasting and irreversible results? In a patient allergic to penicillin, would erythromycin, 500 mg. given every four hours for 30 days, be regarded as satisfactory treatment for tertiary syphilis? What would be recommended as alternative therapy?*

David N. Shapiro, M.D.
Johannesburg, South Africa.

Answer.—There is no way of differentiating serologically between lesions of tertiary syphilis and yaws. The Treponema pallidum immobilization test has so far revealed no essential immunogenic differences between the treponemes of syphilis and yaws (Grin, *Bull. World Health Organ.* **15**:959, 1956). Some clinical differentiations between them are well outlined by Furtado (*A. M. A. Arch. Dermat.* **76**:446, 1957). Penicillin is the treatment of choice in yaws. In Haiti, 258 patients with early yaws were "cured" with sterile procaine penicillin G with aluminum stearate suspension. Injections of 1 cc. at 12-hour intervals were given for four days for a total of 2,400,000 Oxford units. Rein stated, "There are no proven instances of either clinical re-infection or relapse in the patients followed for one year" (*Ann. New York Acad. Sc.* **55**:1179, 1952).

Benzathine penicillin G, the delayed and long-acting penicillin, may give similar results with 1,400,000 units. Smith and co-workers (*Bull. World Health Organ.* **15**:1087, 1956), in a follow-up report after two years of treatment of early syphilis, found that one injection of 2,400,000 units of benzathine penicillin G produced a higher clinical and serologic cure than 4,800,000 units of procaine penicillin G with aluminum stearate suspension given in two to four sessions. Benzathine penicillin G also gave "satisfactory" clinical and serologic results in

the late cases of yaws observed by Furtado. The results of treatment of yaws with broad-spectrum antibiotics are inconclusive, but apparently these are not as effective as penicillin.

Ampofo and Findlay (*Tr. Roy. Soc. Trop. Med. & Hyg.* 44:311, 1950) treated six children with secondary yaws with orally given oxytetracycline. They received either three or four capsules twice daily for seven days, for a total of 10.5 to 14 Gm. Darkfield examinations became negative within 24 to 36 hours, and healing of the lesions was complete in one to four days. Three months after the completion of therapy, all had shown a reduction in titer on serologic testing but none attained seronegativity. Oxytetracycline apparently exerts only a bacteriostatic effect, in contrast to the bacteriocidal effect established for penicillin.

Erythromycin, although not used extensively, appears to be as effective in syphilis and yaws as the other antibiotics, such as chlortetracycline and oxytetracycline. Furtado mentions erythromycin as one of the antibiotics which have been proved effective clinically and serologically in the treatment of yaws. Thomas (*J. A. M. A.* 162:1536-1539 [Dec. 22] 1956) and Olansky and Garson (*A. M. A. Arch. Dermat.* 77:476, 1958) found that the broad-spectrum antibiotics given in 1-Gm. doses every six hours for seven days were as effective as penicillin for treatment of early syphilis. In latent and late syphilis, similar doses are given for 15 days and in neurosyphilis for 30 days. Half of that amount may be given in twice the number of days if the patient can not tolerate 4 Gm. of the antibiotic a day. Oxytetracycline is better tolerated than chlortetracycline. From these reports, it is evident that 90 Gm. of erythromycin should be considered adequate treatment unless the patient has neurosyphilis, when 120 Gm. would be required. In latent and late syphilis, neurosyphilis, and late lesions of yaws, only symptomatic and clinical results may be expected with adequate therapy, as mentioned, with no reversal in serologic fastness.

MUSCLE CRAMPS

To the Editor:—*What is the cause and treatment of muscle cramps? Is there any relationship between them and the use of calcium in the form of phosphorus or carbonate?*

M. G. Radewan, M.D., Wenatchee, Wash.

Answer.—Practically anything that interferes with the nutrition and gas-exchange of normally innervated skeletal muscle can cause the painful contractions called cramps. This is illustrated by the fact that cramps are seen in both sodium intoxication and sodium depletion and in both oxygen intoxication (as when divers inhale oxygen under pressure) and intermittent claudication (ischemic pain in peripheral vascular disease). It is generally assumed that the calcium ion has a relaxing effect on skeletal muscle, yet it antagonizes the magnesium ion which likewise has a relaxing effect. The calcium ion antagonizes both the inhibitory effects of potassium and the stimulant effects of sodium. The concentration of calcium in the blood is greatly reduced by intravenous injections of phosphoric acid or sodium phosphate, yet rather large doses of these two substances are necessary in order to induce tetany. These conflicting facts of experiment do not afford a secure basis for preferring phosphate-free compounds of calcium in the treatment of muscle cramps. There are some products on the market which have been promoted for preventing muscular spasms in pregnancy and which contain the calcium in the form of carbonate or lactate. But it remains to be proved that these phosphate-free compounds, as sources of calcium, are better than calcium phosphate. In elderly patients the most common cause of muscular cramps at night is impaired circulation through the muscles, and the logical treatment is active and passive exercise with or without the use of such vasodilator drugs as ethyl alcohol, theobromine sodium acetate, and nylidrin hydrochloride.

REMOVAL OF IMBEDDED TICKS

To the Editor:—*Please advise on suitable methods to prevent dog ticks from becoming attached to the skin while a person is in brush and weeds. Once the pests are imbedded, how should they be removed without leaving the parasite's body in the skin? Is there any effective antipruritic?*

Harold R. Peasley, M.D., Des Moines, Iowa.

Answer.—The best way to prevent tick bites is to avoid heavily infested areas during the spring and summer months. If one must venture into these areas, protective clothing with elastic at the openings and high boots should be worn. The openings of the clothing or the entire garment may be sprayed with tick repellents. One of the best repellents is *N, N*-diethyltoluamide, which may be obtained in a concentration of 50% in a liquid or 15% in a spray. The U. S. Army has had considerable success with M-1960, which consists of equal parts of *n*-butylactanilide, 2-butyl-2-ethyl-1,3-propanediol, and benzyl benzoate, with 10% polysorbate 80 as emulsifier (Chandler, Parasitology, ed. 9, New York, John Wiley & Sons, 1955, p. 519). While 10% DDT powder is not effective against all species of ticks, it may afford some protection. The body and clothing should be inspected twice a day, if possible, for ticks. Ticks may be removed by touching them with the end of a lighted cigarette, by coating the tick with fingernail polish or petrolatum, or by grasping the tick with a pair of forceps and twisting the head and mouth parts free. Care should be taken not to crush the tick lest the infectious contents be spilled into the wound. Paint the

bite with an antiseptic—iodine tincture is a good one. Antihistamine ointments may produce some antipruritic effects when applied to the bites.

DESENSITIZATION OF RH-NEGATIVE MOTHER

To the Editor:—*About one year ago there was an article concerning a haptene that was being experimentally used to desensitize the* **Rh***-negative mother during pregnancy and the newborn infant. Has this substance been developed further? Is it commercially available, and if so, from whom? Are there any recommended prophylactic measures other than hesperidine and ascorbic acid?*

A. D. Heetderks, M.D., Bozeman, Mont.

Answer.—Many years ago it was shown that the so-called Rh haptene had no specific activity in in vitro tests and that the injection of this material had no effect on the degree of sensitivity of the mother during the pregnancy or on the newborn infant. Hesperidine and ascorbic acid have also been found to be of no real value in such cases, although the use of vitamin C and other vitamins is generally recommended as part of the management of all expectant mothers. In fact, there is no known prophylactic measure of value for treating sensitized expectant **Rh**-negative mothers. The only treatment of established value is exchange transfusion on the baby, which, of course, can be applied only after the baby is born. For fuller details, the following reference may be consulted: Wiener, "An Rh-Hr Syllabus" (vol. 9, Modern Medical Monographs, New York, Grune & Stratton, Inc., 1954).

CATARACT SURGERY

To the Editor:—*What are the schools of thought pertaining to the indications for removal of a cataract which has not ripened to maturity? Also, would it be advisable to remove an unripened cataract from one eye, with the best corrected visual acuity of 20/200 or less, in a person who is blind in the opposite eye as a result of injury or any surgical procedure for an eye impairment?*

Joseph Bogan, M.D., Hyattsville, Md.

Answer.—In recent years the question of whether or not to operate on a patient with an immature cataract has become nearly academic. The maturity of the lens has no role in the decision concerning cataract surgery with intracapsular lens extraction for the improvement of vision. Nuclear sclerosis and posterior subcapsular cataract rarely progress to maturity, and most surgeons believe that it is not necessary to carry out artificial procedures either to make the remainder of the lens opaque or to delay surgery. The decision concerning the time of operation is usually related to how much the visual defect interferes with the patient's activities. A housewife may be moderately content with 20/200 vision, while a businessman or physician would find it impossible to carry on with this degree of visual reduction. Generally, blindness in the opposite eye is no indication for delaying surgery once the vision impairment interferes with the patient's activities.

COLORING OF SEMINAL FLUID

To the Editor:—*A healthy, 33-year-old married man has a complaint of flecks, which resemble graham cracker crumbs in color and consistency, in his seminal fluid. Physical examination revealed no abnormality of the urogenital tract. The result of a Papanicolaou smear of prostatic secretion was reported as negative. He had been taking two high-potency multivitamin capsules daily. He states that the discoloration ceased when he stopped taking the vitamin capsules. Is there any possible connection between the "flecks" in the seminal fluid and the large amount of multivitamin and mineral ingested?*

L. J. Steffan, M.D., Plymouth, Wis.

Answer.—A thorough search of the recent literature has failed to yield any information relative to the "graham cracker flecks" found in the semen. Normal semen is known to contain lecithin, cholesterol, and phosphorized fat. Whether an increase in these constituents after the ingestion of high-potency multivitamin capsules could produce such bodies cannot be answered. This consultant is aware of many unpublished reports of the coloring of semen by a variety of medicaments, but all of these await confirmation.

ALLERGY TO PENICILLINASE

To the Editor:—*Please furnish information regarding the toxic and allergic reactions induced by the use of penicillinase. What is its value in treating an immediate reaction to penicillin?*

M.D., California.

Answer.—This consultant has heard specifically of at least two reactions to penicillinase; these were in the nature primarily of fever and toxic effects resembling reactions to foreign protein rather than anaphylactic shock. Febrile reactions are also mentioned by Dr. M. C. Zimmerman in his published articles. The major consideration, of course, is that penicillinase is an enzyme, and therefore a protein, and that the likelihood of allergic reactions must be anticipated, possibly on the first administration but more likely after repeated administration in the same individual. Penicillinase does not work fast enough to be of appreciable value in the treatment of immediate reactions to penicillin. It may be of value in delayed reactions.

SEASONAL ALLERGIC RHINITIS

To the Editor:—*Is the incidence of complications increased, decreased, or the same after the treatment of uncomplicated seasonal allergic rhinitis (i. e., no asthma or polyps) with antihistamines alone, as compared to that with hyposensitization? Mothers are not anxious to commit themselves to a protracted schedule of regular visits, especially when the children are fearful of injections. Is there any harm in advising treatment with the antihistamine which gives satisfactory relief and waiting until the child is older and more able to cooperate and understand the reason for frequent injections?*

M.D., New Jersey.

Answer.—Evidence that the use of antihistamines in hay fever diminishes or increases the likelihood of such complications as asthma or polyposis is not conclusive. However, the incidence of asthma in persons sensitive to ragweed pollen is about 35% or 40%, and desensitization is effective in preventing the patient with simple hay fever from developing asthma. Thus, it is not the use of antihistamines but rather the omission of desensitization which is the important issue.

DIABETES AND RETINAL HEMORRHAGE

To the Editor:—*A diabetic patient, taking one tablet of tolbutamide daily, had a retinal hemorrhage. Is it possible that this was caused or precipitated by the drug?* *M.D., New York.*

Answer.—As far as is known, there is no evidence to date to indicate that the taking of tolbutamide would cause or precipitate a retinal hemorrhage. Unfortunately, such hemorrhages occur frequently in patients with diabetes, particularly after 10 or more years' duration of the disease. There is considerable evidence to suggest that retinitis occurs earlier and more severely in patients whose diabetic condition has not been well controlled. Some have raised the question as to whether, over many years of the presence of diabetes, sulfonylurea compounds will protect the patient against vascular complications as well as insulin does. However, the answer to this must await the passage of time.

RECURRENT NIGHT SWEATS

To the Editor:—*In the Oct. 11, 1958, issue of* The Journal, *page 843, is a request for advice concerning night sweats. In one treated patient, propantheline bromide was not effective but methantheline bromide, 100 mg., gave complete control. Before the drugs are used, tests must be done to rule out any infection.*

J. W. Robinson, M.D.
2686 Locksley Pl.
Los Angeles 39.

To the Editor:—*With reference to the Question and Answer on recurrent night sweats, which appeared in* The Journal, *Oct. 11, 1958, page 843, a relatively rare cause was not mentioned. Autopsies were performed on two patients with pheochromocytoma who had essentially identical histories. The symptom complex as described warrants investigation along this line. One patient, a 28-year-old primipara, complained of drenching night sweats to the extent that she would have to change her bedclothes several times each night. This began at the third month of pregnancy and persisted to the time of delivery, which was performed by cesarean section because of preeclampsia. Twelve hours later she went into shock and died. A pheochromocytoma of the left adrenal was found. The second patient was a 40-year-old man who had suffered intermittent severe headaches for 10 years. The diagnosis of pheochromocytoma was considered two years prior to his death. Tests with use of phentolamine at that time gave negative results. He, too, experienced night sweats in the year prior to his death. His death occurred during an acute episode associated with hypertension, marked perspiration, and a shock-like state. Again, autopsy revealed a pheochromocytoma of the left adrenal.*

J. Weinberg, M.D.
3230 W. Franklin Blvd.
Chicago 24.

ISOLATION OF PATIENTS WITH STAPHYLOCOCCUS INFECTION

To the Editor:—*In answer to the question on isolation of patients with staphylococcus infection, which appeared in* The Journal, *Oct. 4, 1958, page 716, the consultant states, "All patients should be masked while they are in the operating room." I believe this should read "All personnel should be masked while they are in the operating room."*

Bruce B. Rolf, M.D.
12300 Wilshire Blvd.
Los Angeles 25.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*This consultant meant that not only the personnel but all patients should be masked while in the operating room. It would be an error to limit it to the personnel, because occasionally a guest doctor, consultant, or medical relative are also privileged in being in the operating room. The statement that "all patients should be masked while they are in the operating room" should be accepted. This leaves no exceptions.*